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PREVALENCE, HEREDITY AND DIAGNOSTIC CONSIDERATIONS

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Premature and Delayed Ejaculation

Prevalence, Heredity and Diagnostic Considerations

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ACADEMIC DISSERTATION

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To Göran & Carita
who have always given so much
and asked for so little in return

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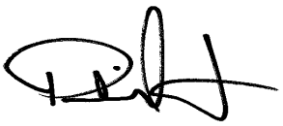

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SAMMANFATTNING PÅ SVENSKA

Ejakulationsstörningar anses allmänt vara en av de vanligaste sexuella dysfunktionerna som drabbar män. Studier har påvisat prevalenssiffror på omkring 30 % i olika populationer, men prevalenssiffrorna fluktuerar mycket beroende på hur man valt att definiera dysfunktionen. Förekomsten av grav prematur ejakulation, där ejakulation alltid inträffar inom en minut från (vaginal) penetration, har dock uppmätts hos omkring en och en halv procent av den manliga befolkningen. Försenad, eller helt utebliven ejakulation, är betydligt ovanligare och anses drabba omkring en procent av alla män. Etiologin bakom prematur och försenad ejakulation är fortfarande oklar, men man anser idag att prematur ejakulation har en neurobiologisk komponent som går att behandla med s.k. selektiva serotoninåterupptagningshämmare (dvs. antidepressiv psykofarmaka). Försenad ejakulation antas i huvudsak uppstå som bieffekt av olika mediciner eller droger, samt sekundärt som komplikation till fysiskt trauma (i synnerhet på ryggraden) eller olika kirurgiska ingrepp, men psykologiska orsaker har också visat sig vara associerade. Etiologin bakom försenad ejakulation är inte heller helt klarlagd.

Den föreliggande avhandlingens mål var att utforska olika aspekter av ejakulationsstörningar och deras etiologi i ett populationsbaserat urval av finska tvillingar, samt deras syskon. Dessa aspekter innefattade prevalens av prematur och försenad ejakulation i den finska befolkningen, samt en kartläggning av etiologiska faktorer bakom ejakulationsstörningar (t.ex. genetiska-, omgivnings- och kontextuella effekter, ålderseffekter och effekter av parförhållandets längd). Undersökningen utfördes i enkätform. Ejakulationsfunktionen mättes empiriskt med tio variabler som fokuserade på olika aspekter av ejakulativ funktion (däribland ejakulationens latenstid, subjektiv uppfattning om kontroll över ejakulationsreflexen och huruvida den tillfrågade vidtagit några åtgärder för att inte ejakulera för tidigt). Dessa variabler faktoranalyserades och på basis av faktoranalysernas resultat konstruerades två summavariabler som mätte prematur och försenad ejakulation. Deltagarna i undersökningen fick också besvara frågor gällande variationer i och frekvens av sexuellt beteende samt frågor rörande sexuella dysfunktioner vid det första samlaget.

Datainsamlingen skedde i två faser. I den första fasen kontaktades 5000 manliga tvillingar i åldern 33-43 år, av vilka 1313 personer besvarade enkäten (27 %). I den andra fasen kontaktades 11914 män. Denna besvarades av sammanlagt 2660 tvillingar (33,7 %) i åldern 18-33 samt deras 18 år fyllda syskon (1263 personer; 31,5 %). Den totala svarsprocenten efter sammanslagning av båda datainsamlingarnas deltagarantal var sålunda 30,8 %.

Såväl prematur som försenad ejakulation visade sig ungefär lika prevalent i Finland som i tidigare studier utförda i andra länder. Detta gällde oavsett definition, så att om prematur ejakulation definierades som en alltid förekommande ejakulationslatens på en minut eller mindre var prevalensen något lägre än två procent, vilket styrker forskningsresultat från bl.a. Nederländerna, Förenta Staterna och Spanien. En signifikant genetisk effekt på omkring 30 % kunde uppmätas för prematur ejakulation. Denna genetiska effekt visade sig vara tämligen beständig från det första samlaget. Dock korrelerade unika effekter i omgivningen (vilka t.ex. kan vara kontextuella effekter, såsom totalt okänd partner eller berusningsgrad) svagt mellan prematur ejakulation vid det första samlaget och prematur ejakulation uppmätt vid tidpunkten för deltagande i undersökningen, vilket antyder att det i huvudsak är unika, enskilda kausala faktorer som orsakar prematur ejakulation vid det första samlaget. Trots att endast mycket svaga ålderseffekter kunde uppmätas, var grav prematur ejakulation mer än tiofalt vanligare vid det första samlaget, vilket antyder att sexuell oerfarenhet och psykologisk spänning kan ha starka effekter på ejakulationslatenstiden. Inga signifikanta genetiska effekter kunde påvisas för försenad ejakulation. Ejakulationslatenstiden visade sig också påverkas signifikant av både frekvens av sexuellt umgänge och utövande av olika typer av sex (t.ex. oral eller vaginal), så att högre frekvenser av sexuellt umgänge och en mera varierad sexuell repertoar var associerade med längre ejakulationslatenstider. Indicier för kontinuitet hos ejakulationsstörningar kunde också påvisas, men inga metodologiskt robusta longitudinella studier har gjorts för att kartlägga hur ejakulationen fungerar och varierar över tid.

Resultaten diskuterades i relation till den pågående debatten om diagnostiska kriterier för prematur ejakulation. Det föreslogs, att effekten av sexuell erfarenhet på prematur ejakulation bör undersökas och eventuellt tas i beaktande vid fastställande av diagnos. De ejakulationslatenstidsförlängande effekterna av varierat och frekvent sexuellt beteende borde samtidigt undersökas vidare, framför allt för att fastställa kausalitetens riktning i frågan: det kan också vara fallet, att män med naturligt längre ejakulationslatenstider har ett bättre sexuellt självförtroende och därför ägnar sig oftare åt (och mer varierade former av) sex. Molekylärgenetiska studier borde utföras för att kartlägga de gener som ligger bakom den genetiska effekten på prematur ejakulation. Dessa studier kunde sedan ligga till grund för utvecklingen av t.ex. skräddarsydda mediciner för behandling av ejakulationsstörning.

Sammanfattningsvis kunde följande slutsatser dras från resultaten av föreliggande arbete: Prematur ejakulation är tämligen vanligt i Finland om dysfunktionen mäts enligt subjektiv uppfattning hos de drabbade. Om definitionskriteriet istället än en ejakulationslatenstid som understiger en minut från penetration, sjunker

prevalenssiffran till något under två procent. Ejakulationsstörningar har mycket små, men signifikanta associationer med ålder, på så sätt att problematiken ökar med åren. En signifikant genetisk effekt på omkring 30 % kunde uppmätas för prematur, men inte för försenad, ejakulation. Ejakulationslatenstiden uppvisar också en viss association i positiv riktning av ett frekvent och varierat sexualliv.

ABSTRACT

Premature ejaculation is commonly regarded as the most common sexual dysfunction in men. Studies have reported prevalence rates of around 30% in the general population, but prevalence rates fluctuate widely between studies because of discrepancies with regards to definitions and diagnostic criteria. When defined by an intra-vaginal ejaculation latency time of less than one minute, frequency of occurrence is dramatically reduced, and it is estimated that around one and a half per cent of the population exhibit ejaculation latency times of one minute or less. Delayed, or retarded, ejaculation is a lot less common, and is estimated to occur in around one percent of the general population, or even less. The etiology of both premature and delayed ejaculation is still uncertain. Recent research has proposed that premature ejaculation is (strongly) affected by neurobiological mechanisms, and that it is treatable with selective serotonin reuptake inhibitors (i.e. antidepressant pharmacotherapy). Delayed ejaculation is hypothesized to occur as a side effect of (both medicinal and recreational) drugs, as well as secondary to physical trauma, or as a complication of surgery. Psychological factors influencing the etiology of delayed ejaculation have also been proposed. However, not all aspects of the etiology of delayed ejaculation have been charted either.

The aim of the present study was to investigate certain aspects of ejaculatory disorders and their etiology in a large, population-based sample of Finnish twins and their siblings. These aspects include prevalence of premature and delayed ejaculation, as well as analyses of potential etiological factors (e.g. genetic, environmental, and contextual effects that may have an impact on ejaculatory functioning). Effects of age and relationship length on ejaculatory dysfunction were also assessed. Data were collected through a survey, and ejaculatory function was measured empirically with ten variables focusing on different aspects of ejaculatory function and control (e.g. frequency of anteportal ejaculation, ejaculation latency time, whether the participant had taken any measures to prevent premature ejaculation, and subjectively perceived control of ejaculatory function). These variables were subsequently subjected to factor analyses, based on which composite variables measuring premature and delayed ejaculation were formed. Questions regarding premature ejaculation during the first intercourse were also asked of the participants. Finally, they were asked to respond to questions regarding variations in and frequency of sexual activities.

The data collection was completed in two separate phases. In the first phase, 5000 male twins aged 33-43 years were contacted, of which 1,313 replied to the questionnaire (27%). In the second phase, a total of 11,914 men were contacted. Of

these, 2,660 twins (33.7%) aged 18-33 years, and 1,263 (31.5%) of their at least 18-year-old siblings responded to the survey, yielding a total response rate of 30.8% when both data sets were combined.

Premature, as well as delayed, ejaculation had very similar prevalence rates in the sample under study compared to what has previously been reported elsewhere. This was true regardless of definition: for example, if premature ejaculation was defined by an ejaculation latency time of no more than one minute, prevalence rates of less than two per cent were found, replicating findings from, for example, the Netherlands, the US, and Spain. A significant genetic effect explaining around 30% of the total phenotypic variance in premature ejaculation was also detected. Self report of premature ejaculation was found to be relatively stable from the first intercourse to later in life. For the most part, genetic effects mediated this stability. In contrast, unique (or non-shared) environmental effects on premature ejaculation had a very weak correlation between the first intercourse and when measured later in life, indicating that there are unique factors contributing to premature ejaculation during the first intercourse. These could be contextual factors, such as the partner being unknown, or intoxication. Even though only weak effects of age were found in the present study, severe premature ejaculation was more than ten times more common during the first intercourse, compared to later in life, which could be the result of the impact sexual naïvete may have on ejaculation latency time. No genetic effects were detected for delayed ejaculation. Temporal stability was found here as well in the sense that premature ejaculation problems during the first intercourse were negatively related to later delayed ejaculation. Effects of age and relationship length were generally positive, so that problems related to premature ejaculation increased slightly with increasing age and relationship length. Ejaculation latency time was also significantly positively associated with frequency of sexual activities and variations in the ways of achieving ejaculation, with oral and anal sex having the strongest associations. On the whole, variables measuring different aspects of ejaculatory dysfunction had quite weak associations with sexual distress. Altogether, these variables accounted for 16.5% of the variation in sexual distress, implying that more than four fifths of the total variance in sexual distress is accounted for by something other than premature or delayed ejaculation. Variables measuring subjective experience of PE had the strongest associations with sexual distress.

Results were discussed in relation to the ongoing debate on diagnostic criteria for premature ejaculation. It was suggested that effects of sexual experience on premature ejaculation should be investigated, and perhaps, considered when diagnosing premature ejaculation. Ejaculation latency time-improving effects of varied and frequent sexual activity should also be subjects of further study, especially to establish direction of causality: it may also be the case that men with

naturally longer ejaculation latency time are more sexually adventurous, and engage more frequently in sexual behavior. Molecular genetic studies should be conducted to identify the genes that are behind the perceived genetic effects on premature ejaculation. These studies could, then, be a first step in a process of developing genetically tailored drugs to further improve pharmacotherapy of premature ejaculation. Also, properly conducted and well-designed longitudinal studies of ejaculatory function are needed to investigate further how ejaculatory performance behaves over time.

In summary, the present study generated the following key results: premature ejaculation is fairly common in Finnish men, if diagnosed by subjective perception and distress. If diagnosis is done by a one-minute ejaculation latency time, the prevalence is slightly less than two per cent; if by anteportal ejaculation, around one per cent. Ejaculatory dysfunctions have weak, but significant positive associations with age, indicating that problems related to premature ejaculation appeared to increase with increasing age. A significant genetic effect of around 30% could be measured for premature, but not delayed, ejaculation. Ejaculation latency time had some positive association with frequency of and variation in different sexual activities. Associations between experienced sexual distress and premature and delayed ejaculation are generally rather weak.

1 INTRODUCTION

Premature ejaculation (PE) is regarded as a serious disorder with a profound impact on a man's life and partner relations (Hartmann, Schedlowski, & Krüger, 2005). While it is also often quoted as the most common of the male sexual dysfunctions (e.g. Salonia et al., 2009; Frank, Anderson, & Rubinstein, 1978; Wang, Kumar, Minhas, & Ralph, 2005; Montorsi, 2005), it has received fairly little scientific attention until the last few decades. The last 20 years, however, have seen significant advances in the field, both in terms of scientific research and understanding of the condition, and development of therapies (approved pharmacotherapy for PE has, for the first time, been introduced in Finland and its neighboring Sweden as of February 2009, with five more European countries expected to follow suit in the near future; Finnish National Agency for Medicines, 2009). In a recent review study, Rowland and Burek (2007) report an overall increase of published papers related to PE over the past 25 years, and that the emphasis of these papers has shifted towards the pharmacological and biological in recent times, while the number of articles on psychological and behavioral aspects has decreased. However, many issues related to the study and understanding of PE still remain unclear, and there is continued disagreement on several topics. For example, there are ongoing debates over the definition, diagnostic criteria, research methodology and suitable (pharmaco-) therapies (see e.g. Shabsigh & Rowland, 2007; Hellstrom, 2007; Waldinger & Schweitzer, 2007; Waldinger & Schweitzer, 2008a; McMahon, 2008b).

Delayed ejaculation (DE), on the contrary, has been a less popular subject among researchers. Few studies have ever looked into this condition (Rosen, 2000; Richardson, Nalabanda, & Goldmeier, 2006), and comparatively little effort is put into investigating its etiology, or therapy development. However, much like PE, DE is reported to cause its bearers considerable distress and discomfort (Perelman & Rowland, 2006). A predominantly psychogenic etiology to DE has been proposed (*ibid.*), but this view has been challenged in favor of a neurobiological approach, which points to the ejaculation-delaying (or even –inhibiting) potency of certain neurotransmitters (Waldinger & Schweitzer, 2005).

In summary, ejaculatory dysfunctions are complex in nature, and direct causal factors are still largely unknown. The present thesis aimed at exploring ejaculatory dysfunction (with emphasis on PE, but also considering DE) in two large population-based samples of twins and their siblings through survey methods. First, prevalence rates, relationship with age, continuity of the dysfunctions, and etiological issues were investigated and considered. Next, questions related to the diagnostics of ejaculatory dysfunction were addressed.

1.1 Definitions and diagnostic criteria

The attempts to formulate definitions and diagnostic criteria have as a rule not considered the ultimate, evolutionary level of explanation. Instead, all the definitions based on personal experience of a problem, a certain level of distress, ejaculation latency time cut-off, or a certain number of penile thrusts are ultimately subjective, and of arbitrary choice. For a certain temporal property of ejaculation to be ultimately considered as dysfunctional, it must be disruptive of its main purpose which is, in the evolutionary sense, to impregnate the egg, and thus pass on the genes of its carrier. Hong (1984) has proposed the idea that rapid ejaculation is indeed an evolutionary adaptation, and that a swift and responsive ejaculatory reflex has been previously a superior trait. For example, a quickly ejaculating male (primate) will need considerably shorter time to complete copulation and will thus have several advantages over one who takes his time (e.g. he is less likely to be attacked by other aroused males, or repelled by the female). The perception of rapid ejaculation as dysfunctional, Hong continues, only reflects the lag between biological and social changes. In conclusion, it is difficult to conceive of an objective measure (other than perhaps anteportal ejaculation) of how, or when, to define ejaculation as "dysfunctional" in an ultimate sense. It has been suggested that female orgasm would be associated with increased probability of successful conception (Baker & Bellis, 1993). If female orgasm is more likely with longer ejaculation latency times it would imply that a (very) short ejaculation latency time is indicative of dysfunction in an ultimate sense of being harmful from a reproductive perspective. Or, it could be that the amount of sperm in the ejaculate is positively associated with both probability of successful conception and ejaculation latency time, which could also provide proof of short ejaculation latency times constituting a disorder. These are testable hypotheses which have implications for how we think about the etiology of PE: is PE a result of normal variation (or even a positive adaptation), or is it a pathological condition which may be explained by a disturbance in the functioning of the ejaculatory system? A too slow or completely absent ejaculation is, on the other hand, most definitely disruptive of the purpose of ejaculation in the evolutionary sense. Hence, it may be somewhat easier to clinically define and operationalize DE compared to PE. Furthermore, if short ejaculation latency times have served a positive evolutionary purpose, separate etiologies for PE and DE are implied, as DE cannot perceivably be an evolutionary adaptation.

However, as PE (or DE) cause subjective suffering, there is need for treatment based on the best possible diagnostic approach. Formulating and adequate definition for PE (and DE) has turned out to be a major stumbling block in the research of ejaculatory dysfunction. Both are listed in the Fourth Edition of the Diagnostic and Statistical

Manual of Mental Disorders, Text Revision (DSM-IV-TR; American Psychiatric Association, 2000), however with DE named *male orgasmic disorder*.

1.1.1 Definition and diagnostic criteria of premature ejaculation

During the last decades of research, the definition of PE has undergone a formidable metamorphosis. Premature, or "rapid", ejaculation is mentioned already in the 19th century medical literature (see Waldinger, 2004 for a historical review of PE research), however, starting from modern sex research and the Kinsey report (which speculated that around 75% of men would reach orgasm in two minutes; Kinsey et al., 1948), several different aspects of ejaculatory function have been investigated in the pursuit of a universally acceptable definition of PE. In the classic study by Masters and Johnson (1970), a man ejaculating prior to his partner reaching orgasm in more than 50% of intercourses was classified as dysfunctional. Other approaches have focused on subjective experience of PE (Laumann et al., 2005), perceived degree of ejaculatory control (Porst et al., 2007), experienced distress (also of partner) resulting from ejaculatory performance (*ibid.*), and latency time from intromission to ejaculation (Waldinger, 2005a), but also frequency of occurrence of (self-perceived) PE, occurrence of anteportal ejaculation, amount of penile thrusts managed before ejaculation (see e.g. Grenier & Byers, 1997). It should be pointed out, that even though some studies may have used the same indicator for measuring PE (e.g. ejaculation latency time), their results are not necessarily directly comparable, because of discrepancies in the reporting of the results and the cut-off scores used for the different measures. For example, where some studies have used an ejaculation latency time of one minute as a cut-off for diagnosis (e.g. Cooper & Magnus, 1984; Segraves, Saran, Segraves, & Maguire, 1993), others have used two (Strassberg, Mahoney, Schaugaard, & Hale, 1990) while others still have used a cut-off score of up to seven minutes (Schover et al., 1982), or indeed anything in between (see McMahon et al., 2008). In addition, two studies may both focus on the ejaculation latency time aspect of PE, but the first may report the frequency of which a stopwatch timed ejaculation latency time of less than some cut-off score, while the other study may report self-perceived ejaculation latency times on a five-grade Likert scale.

The widely used Diagnostic and Statistical Manual for Mental Disorders (DSM-IV-TR; American Psychiatric Association, 2000) defines PE as "*a persistent or recurrent ejaculation with minimal sexual stimulation before, on, or shortly after penetration and before the person wishes it*". Furthermore, it is stipulated that the condition "*must also cause marked distress or interpersonal difficulty*" and that it "*is not due exclusively to the direct effects of a substance*". This definition has been the subject of criticism in the literature of late, for being perceived as empirically imprecise, for its lack of a quantitative

measure of ejaculatory functioning (see e.g. Segraves & Balon, 2007; Waldinger, 2005b), and also for causing overestimation of prevalence rates and discrepancy between studies, as it cannot separate between subjective complaints and definite dysfunction (e.g. Patrick et al., 2005; Waldinger & Schweitzer, 2008b). Several scholars have also advocated the removal of the explicit requirement of personal or interpersonal distress from the diagnostic criteria of PE, or indeed, sexual dysfunctions altogether (e.g. Segraves, Balon, & Clayton, 2007; Waldinger & Schweitzer, 2006). Furthermore, as argued by Patrick and his colleagues (2005), the DSM-IV-TR definition also fails to correctly diagnose PE patients if they do not perceive their rapid ejaculation as a problem, or are not psychologically or emotionally affected by it. However, voices have also been raised in defense of the DSM-IV-TR definition (e.g. Hellstrom, 2007), as it is multi-factorial in nature and "*encompass aspects of the condition that patients describe as important*" (Shabsigh & Rowland, 2007, p. 1468). Furthermore, definitions have also been proposed by other influential bodies, such as the American Urological Association (Montague et al., 2004) and the World Health Organization (WHO), which in their International Classification of Diseases (ICD-10) of 1993 defined PE as "the inability to control ejaculation sufficiently for both partners to enjoy sexual interaction", thus putting emphasis on the control aspect of ejaculation. The ICD-10 is in general use among physicians in Finland.

In the last decade, classification of PE into different subtypes has been proposed in the scientific literature. The concept in itself is, however, not new. In 1943, Schapiro proposed a division of PE into "type B" (or *primary*), and "type A" (or *secondary*) subtypes, with the "type B" subtype being a chronic, severe kind and "type A" more contextual in nature and leading to erectile dysfunction. Subsequently, this classification has been introduced and adapted by Waldinger (2007a) and extended to four different subtypes with different etiologies (and, thus, requiring different treatments): "life-long PE" (primary PE), characterized by a permanent, life-long PE in nearly every intercourse, with so-called intra-vaginal ejaculation latency times (IELTs) of about a minute or less. This subtype is hypothesized to have a "genetic" or "neurobiological" etiology. The second subtype, "acquired PE" (secondary PE), differs in that the condition is developed at some point in the patient's life. "Acquired PE", hypothetically, has a psychological or social etiology (i.e. may be related to relationship problems), or may occur secondary to a somatic illness or dysfunction, such as erectile dysfunction or prostatitis (McMahon, 2008a). In addition to these two, Waldinger (2007a) mentions two additional subtypes, which differ from the previous two in that they are not actual sexual dysfunctions, but normal (with regards to IELT) ejaculatory function that is (mis)perceived as dysfunctional and problematic by the patient. As such, "natural variable PE" (characterized by quite normal IELTs with random, inconsistent situational

experiences of rapid ejaculation) and "premature-like ejaculatory dysfunction" (where the patient simply misperceives his fully normal or even very long ejaculation latency), does not require pharmacological treatment – psycho-education, reassurance and psychotherapy has been suggested as sufficient treatment (Waldinger & Schweitzer, 2006). In terms of frequency, the latter two are thought to be more common than the two more severe subtypes (McMahon, 2008a), however, no studied have been conducted to readily differentiate between the subtypes.

Recently, in the wake of the growing criticism of the DSM-IV (and other "authority-based") definition (McMahon et al., 2008; Waldinger, 2004; 2005b; Waldinger & Schweitzer, 2006; Waldinger & Schweitzer, 2008b), a definition of lifelong PE was unanimously agreed upon by an *ad hoc* committee assembled by the International Society of Sexual Medicine (ISSM; McMahon et al., 2008). The committee defined lifelong PE as follows (p. 1593):

"Lifelong PE is a male sexual dysfunction characterized by

- *ejaculation that always or nearly always occurs prior to or within about one minute of vaginal penetration;*
- *the inability to delay ejaculation on all or nearly all vaginal penetrations; and*
- *negative personal consequences such as distress, bother, frustration, and/or the avoidance of sexual intimacy."*

This definition marks a shift in theoretical approach towards a definition centered around intra-vaginal ejaculation latency time (IELT). The tendency to rely heavily on IELT measures has also been met with some skepticism, in that it is potentially an as imprecise and unvalidated proxy measure as any other, for not taking the experiential aspect of individuals suffering from PE into account (Shabsigh & Rowland, 2007; Shabsigh, 2006; Steggall & Pryce, 2006), and for excluding men ejaculating *ante portas* (before penetration). Other studies have suggested that patient-reported outcomes (PROs), in addition to IELT measures, are required to correctly define and diagnose PE (Patrick et al., 2005). Shabsigh and Rowland (2007) argue, that time in itself is not causal of ejaculation, but stimulation over time is. As such, IELT is "*relevant only insofar as it assumes a certain amount of penile stimulation (or thrusting)*", (p. 1470). Furthermore, this definition is almost exclusively based on the results of studies on vaginal intercourse in heterosexual couples, which has implications for its generalizability if, for example, homosexual individuals differ in any way from heterosexual individuals in their ejaculatory functioning. Recently, the ISSM assembled another *ad hoc* committee to formulate a definition of acquired PE; however, the members of this committee are yet to agree on this definition.

In summary, although significant strides towards a more uniform agreement on a suitable definition, and adequate diagnostic criteria, for PE have been taken in recent years, some crucial problems with regards to the definition of PE still persist, and researchers continue to approach PE from a variety of different theoretical and methodological angles. The main obstacle is still to find an agreement on "how quickly is too quickly", and to decide whether a man or his relationship suffers due to the condition (because there is not enough time for his partner to be satisfied). The latter raises the question whether it is the distress of the man – or that of his partner – that is indicative of the dysfunction (partners of men diagnosed with PE have been shown to report significantly more distress than partners of men not diagnosed with PE; Patrick et al., 2005). Again, the difficulty in formulating a clinically and scientifically suitable definition of PE on an ultimate causal level is evident in the debate.

1.1.2 Definition and diagnostic criteria of delayed ejaculation

DE, also often termed Male Orgasmic Disorder (American Psychiatric Association, 2000; Richardson, Nalabanda, & Goldmeier, 2006) is significantly less debated than PE, but defining DE suffers from many of the the same problems as defining PE. In the DSM-IV-TR (American Psychiatric Association, 2000), DE is defined as *"the persistent or recurrent delay in, or absence of, orgasm after a normal sexual excitement phase during sexual activity that the clinician, taking into account the person's age, judges to be adequate in focus, intensity, and duration. The disturbance causes marked distress or interpersonal difficulty. The orgasmic dysfunction is not better accounted for by another Axis I disorder (except another Sexual Dysfunction) and is not due exclusively to the direct physiological effects of a substance (e.g. a drug of abuse, a medication) or a general medical condition"* (pp. 552). Waldinger and Schweitzer (2005) point out that, unlike the DSM-IV-TR definition of PE, the definition of DE is centered around *orgasm* (and not *ejaculation*) which, they continue, "*is not in line with current neurobiological views*" (p. 77). Waldinger and Schweitzer point out that orgasm and ejaculation are completely separate entities, and that a definition should be concentrated around the difficulty to achieve ejaculation, as the (neurobiological) etiology of ejaculation is better understood. In their view, DE can be viewed as a mirror image of PE, albeit on the opposite side of the ejaculation latency time distribution and as such, DE can also be classified into different subtypes such as "lifelong" and "acquired". Finally, it should perhaps be noted that while the study of PE can be centered around ejaculation latency time, it is hardly meaningful to build a useful definition of DE on a specific ejaculation latency cutoff.

1.2 Prevalence of premature and delayed ejaculation

As a result of the difficulties related to the definition of PE (and DE), prevalence estimates of PE have varied widely in the literature, with some studies suggesting that up to 60% (Reading & Wiest, 1984), or even as many as 75% (McMahon, 1998), of all males could experience PE-related problems from time to time, or at some point in their lives. In a review of recent studies, however, Montorsi (2005) suggests a global prevalence of PE of around 30% across age groups and different cultures. A recent internet survey of 12,133 men aged 18-70 in the United States, Germany and Italy yielded similar figures, with a mean PE prevalence rate of 22.7% based on self-report measures (Porst et al., 2007). However, if (stop-watch timed) IELTs – as opposed to subjective reports of research participants, or complaints of patients at urology clinics – are employed as the main criterion for definition, prevalence rates decrease dramatically. For example, in a multinational population survey published in 2005, a threshold IELT of 1 minute yielded a prevalence rate of less than one per cent; and an IELT percentile of 0.5 (i.e. the 0.5 % of the sample with the shortest IELTs) resulted in a IELT threshold of 0.9 minutes (Waldinger, Quinn et al., 2005). Waldinger (2007a) argues, that subjective experiences of PE symptoms are common in men, and that such experiences *per se* are not sufficient to diagnose a patient with definite PE (i.e. patients that can be classified as suffering from "lifelong" or "acquired" PE) – only those with exceptionally short IELTs should be diagnosed and receive medical treatment.

Research focused on anteportal ejaculation is scarce, although individuals ejaculating *ante portas* are included in studies of men with severe (lifelong) PE. Often, these men are not treated separately and prevalence figures of anteportal ejaculation are lost as these individuals are coded into the same group as, for example, men with an IELT no greater than 30 seconds. However, McMahon (2002) reported that 5.6% out of a sample of 1,346 patients with (severe) PE predominantly ejaculated anteportally. In support of this, Waldinger and Schweitzer (2008a) note that cases in which men suffering from chronic anteportal ejaculation are "extremely rare" (p. 995).

The prevalence of DE has generally been reported to be rather low (Rowland, van Diest, Incrocci, & Slob, 2005). Studies have estimated DE to appear with a frequency of 1-4% in sexually active men (Jannini, Simonelli, & Lenzi, 2002; Jannini & Lenzi, 2005; Perelman & Rowland, 2006), while Nathan (1986) found a prevalence rate of a mere 0.15% in the general male population. Waldinger and Schweitzer (2005) conclude that DE "*always appears the least expressed sexual complaint*" (pp. 77-78).

1.3 Etiology of premature and delayed ejaculation

While having historically been, more or less, regarded as a strictly "psychological" condition, the idea of a "biological" etiology to ejaculatory dysfunction has steadily been increasing its popularity in the literature (Waldinger, 2002; 2004). A non-biological approach was still strongly emphasized around 40 years ago by Masters and Johnson (1970), who argued that PE was a learned behavior, resulting from early, hurried sexual experiences, and that the condition could be treated accordingly with behavioral therapy. However, starting with Schapiro's landmark paper in 1943, where he postulated PE to be a "psychosomatic" condition, the last two decades have seen a massive increase in publications describing, or indeed assuming, a (neuro)biological/genetic etiology to both premature (e.g. Donatucci, 2006; Waldinger, 2002; Waldinger & Olivier, 2005) and delayed (Waldinger & Schweitzer, 2005) ejaculation. In addition, it is well established that ejaculation is a reflex, and that this reflex is completed by components in the lumbosacral spinal cord (Truitt & Coolen, 2002). For example, the ejaculatory reflex is intact in most men with spinal cord injury (dependent, among other things, on the location of the injury), and can be evoked by stimulation (electrically or by intense penile vibration; Brackett et al., 1998). However, what exactly triggers this reflex is still largely unknown.

This shift towards a neurobiological approach has recently, in turn, spawned plenty of studies testing the effects of drugs (particularly selective serotonin-reuptake inhibitors, SSRIs, and tricyclic antidepressants) on PE (e.g. Eaton, 1973; Segraves, Saran, Segraves, & Maguire, 1993; Waldinger, Hengeveld, Zwinderman, & Olivier, 1998a; Pryor et al., 2006). An integrated approach has been suggested by Rowland and Motofei (2007), who have criticized the dichotomization of PE into "biological" vs. "psychological" for being counter-productive and misguided, instead proposing a view that ejaculatory response is a complex system of integrated, "hard-wired" (e.g. reflexive, genetic) and "soft-wired" neurophysiology (e.g. brain-level, experience-based, psychological constructs); a system of peripheral and central responses, of which *"some are modifiable* (i.e. softwired), *others not"* (p. 77). These cannot be readily separated into distinct "biological" or "psychological" components and as such, they argue, a dichotomous approach will be less effective in the pursuit of therapeutic outcomes. While DE has been proposed to have a predominantly psychogenic etiology, approaches integrative of biogenic and psychogenic etiologic factors have also been proposed for DE (Perelman & Rowland, 2006). Furthermore, DE is often reported to occur secondary to drug treatment (or abuse), various medical conditions and as a complication of surgery (Segraves, 1989; Rosen, 2000).

1.3.1 Genetic factors

A hereditary component in PE was suggested already in 1943 by Schapiro, who noted that PE patients after questioning often *"[...] elicited the information that relatives of the patients (father or brother) had suffered from the same disorder. Thus, we may assume that in this group, heredity may play a part in the etiology."* (p. 376). Little attention was paid to this finding until 1998, when Waldinger and his colleagues found that the odds that PE would co-occur between family members were significantly higher than what could be expected from prevalence rates in the population. In their study, 14 PE patients with a total of 11 of their relatives were clinically interviewed and diagnosed (with an additional six relatives submitting information of family history, adding up to a grand total of 17 relatives). They found that 91% of the 11 relatives of PE patients eligible for interview and diagnosis suffered from lifelong (or primary) PE themselves. This finding led the authors to conclude that genes play a part in the development of PE, in that the frequency of occurrence between family members was much higher than in the general population (Waldinger, Rietschel, Nöthen, Hengeveld, & Olivier, 1998). While plausible, familial resemblance in itself cannot prove genetic influence, because genetically related individuals also most often share their environment to some extent. Therefore, shared environmental factors could also explain familial occurrence of PE. By conducting twin studies, however, the shared environmental component contributing to the variance in a trait can be separated from the additive genetic component (readers are advised to consult the Method section 3.3 for a detailed description of quantitative genetics and twin research methodology). Furthermore, the hypothesis of a genetic etiology to PE gains support from the association of PE with, for example, serotonergic transmission: an association between genes and neurotransmitters is well established (e.g. Lesch, 2003). Recently, Janssen et al. (2009), in a study of 89 patients and 92 controls, found a polymorphism of the serotonin transporter promoter region *5-HTTLPR* to be significantly associated with IELT in a sample of Dutch men, however, there was no group difference between men diagnosed with lifelong PE and controls. In other words, no significant difference in allele frequencies between the groups was detected, but within the PE group, those with two copies of the long allele of the *5-HTTLPR* had significantly shorter IELTs than those with one or two copies of the short allele (geometric mean IELTs were reported as 13.2, 25.3, and 26.04 seconds for the long/long, short/long, and short/short alleles groups, respectively). The individuals in the study group were not matched with regards to age and marital status to the individuals constituting the control group. In summary, the results of preliminary studies have been encouraging, but a definite genetic association with ejaculatory dysfunction has not yet been established. This is, to date, the only molecular genetic study on ejaculatory function conducted on humans. There are no

studies that have directly attempted to establish a potential genetic etiology to DE, but a heritable component is implicitly assumed also for DE according to the ejaculation distribution theory of Waldinger and Schweitzer (2005).

Differences in ejaculation latency times between participants from different countries have also been observed (Waldinger, Quinn et al., 2005), a finding that may be explained by differences in the frequencies of alleles affecting PE between different human populations. However, sociocultural differences could also cause the observed difference in IELTs. The causal mechanism behind these results is unknown.

1.3.2 Biological correlates

What is presently known about the functional neuroanatomy of ejaculation stems, foremostly, from a handful of studies on male rats (Veening & Coolen, 1998; Coolen, Peters, & Veening, 1996; Coolen, Olivier, Peters, & Veening, 1997; Truitt & Coolen, 2002). As shown by Coolen and his colleagues, there are several brain regions that undergo distinct activation in relation to ejaculation, and more importantly, a group of cells in the lumbar spinal cord that appear to play a pivotal role in the generation and regulation of ejaculation (Young, Coolen, & McKenna, 2009). This group of cells relays ejaculation-related signals from the genitals to the brain, expressing neurokinin-1 receptors. Removal of these neurons resulted in complete disruption of ejaculation (in rats), while other aspects of sexual behavior (such as mounting frequency and behavior) remained intact (Truitt & Coolen, 2002). Studies conducted on rats also led Waldinger (2005c) to hypothesize that hyperfunction of the 5-HT_{1A} receptor and/or hypofunction of the 5-HT_{2C} receptor is associated with PE, whereas the inverse is associated with DE. Neurophysiological differences in rats divided into groups based on their ejaculation latency times were also recently observed by Borgdorff et al. (2009). Clinical trial studies, in which drugs have been tried to treat PE have also provided valuable knowledge of the neurobiology of ejaculation. For example, results from trials involving antidepressants, particularly tricyclic (e.g. clomipramine; Eaton, 1973; Segraves, Saran, Segraves, & Maguire, 1993) and serotonergic (SSRIs; e.g. Waldinger, Berendsen, Blok, Olivier, & Holstege, 1998; Meston & Gorzalka, 1992) drugs suggest involvement of the serotonergic system in ejaculatory functioning, as medication has been found to delay ejaculation significantly. The results of a meta-analysis of 35 studies with serotonergic antidepressants thus led Waldinger (2002) to conclude that PE is "*a neurobiological phenomenon related to central serotonergic neurotransmission and likely influenced by hereditary factors*" (p. 2359). However, antidepressants have proven side effects such as reduced libido and sexual satisfaction (Corona et al., 2009). While there is clearly

an ejaculation-delaying potency in antidepressants, ejaculation latency time is not necessarily the optimal measure of PE if sexual enjoyment of the man is to be considered in the analysis of treatment outcomes. However, if increasing the sexual satisfaction of the partner by increasing ejaculation latency time is the primary purpose of the treatment, the negative side effects may be acceptable.

In the case of DE, correspondingly, Waldinger and Schweitzer (2005) propose that ejaculation should be viewed as a continuum of ejaculation latency time (the *ejaculation distribution theory*, Figure 1) and that DE, as such, is a neurobiological phenomenon on the opposite side of the latency time distribution, but nonetheless affected by the serotonergic system (and thus, genetic makeup). Also, they continue, several neurotransmitters have been found to delay (or even inhibit) ejaculation. In their review study, Clayton and Shen (1998) found that psychotropic drugs often have ejaculation-delaying or –inhibiting effects, while evidence for any drugs with reverse (i.e. ejaculation-inducing) effects remains anecdotal. There is also some evidence for (significant) dopaminergic involvement in ejaculatory function, but its specific role remains unclear (Andersen & Tufik, 2005).

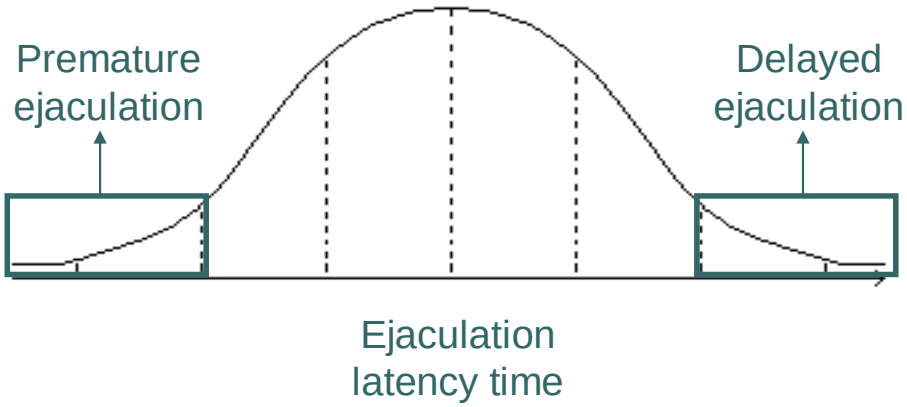

Figure 1. The ejaculation distribution theory, which postulates that ejaculatory dysfunction is the result of normally distributed ejaculation latency time in the population, with individuals on either extreme of the distribution affected by either premature, or delayed, ejaculation (Waldinger & Schweitzer, 2005). Genetic and neurobiological effects are hypothesized to be causal of ejaculation latency times at either end of the distribution curve.

Recently, evidence for endocrine involvement in ejaculatory function has emerged in the literature. Corona and his co-workers (2008) found that PE patients reported higher levels of testosterone, and older participants (55-70 years) diagnosed with DE displayed significantly lower testosterone levels compared to PE patients and controls. Furthermore, PE patients showed the lowest, and DE patients the highest, prevalence of hypogonadism in their sample. They conclude that testosterone may

play a facilitatory role in the control of the ejaculatory reflex, and propose that DE may be treatable with administration of androgens.

A direct peripheral (i.e. not directly related to the central nervous system) etiology of PE, namely hypersensitivity of the glans penis, has also been given some consideration (e.g. Xin et al., 1996), however, positive results of such studies have been disputed. For example, Vanden Broucke et al. (2007) found no correlation between penile sensitivity measurements and ejaculation latency time. Nevertheless, the idea of (hyper)sensitivity as a causal agent of PE is the rationale for the quite common practice of topical treatments for PE, and indeed, topical treatments have been found to delay ejaculation significantly in clinical trials, and several desensitizing agents are for sale on the market (Morales, Barada, & Wyllie, 2007). In addition, circumcision status has been proposed to affect the sensitivity of the penis. In most studies, circumcision status does not appear to affect ejaculation latency time or ejaculatory performance (e.g. Collins et al., 2005; Kigozi et al., 2006; Waldinger, Quinn et al., 2005). However, some indications of both ejaculation-delaying and ejaculation-inducing properties of circumcision have been published recently. In a study of Turkish men, having been circumcised was associated with a slight increase in ejaculation latency time (Senkul et al., 2004), thus indicating some desensitizing effects. Nevertheless, a multi-national population survey (in which all participants from Turkey were circumcised) found significantly shorter IELTs in Turkish men compared to participants from western countries, where circumcision is not nearly as common (Waldinger, Quinn et al., 2005). However, in the latter study circumcision status and population of origin were confounded which makes it difficult to draw any conclusions regarding the effects of circumcision as such. In a study conducted in Kenya, circumcised men reported increased sensitivity of the penis, and rating the ease with which they were able to achieve orgasm as "much" better (Krieger et al., 2008), which lends some support to the view that circumcision may increase likelihood of PE at least in the short term. In summary, no inconclusive evidence for either ejaculation-delaying or –inducing effects of circumcision have been proven, and there is uncertainty whether PE can be caused by peripheral-physiological differences in penile sensitivity. However, some topical desensitizers do have significant ejaculation-delaying effects, suggesting that variations in peripheral nervous activity could play a part in the etiology of ejaculatory dysfunction.

An association between PE and some neurological disorders, physical trauma such as spinal cord injury (especially if affecting the conus medullaris), acute bacterial prostatitis (Fasolo, Mirone, Gentile, Parazzini, & Ricci, 2005), and the use of certain drugs (Clayton & Shen, 1998) has also been postulated. In the case of DE, ejaculation-delaying effects of anti-adrenergic and neuroleptic drugs, and an association with various surgical or medical conditions (such as multiple sclerosis) have also been

proposed as causal factors of DE by Segraves (1989) and Rosen (2000). Hyperfunction of the 5-HT2C (and/or hypofunction of the 5-HT1A) receptor have also been proposed as potential causal agents for DE (Waldinger, 2005c). Alcohol has also been found to delay ejaculation (Malatesta, Pollack, Wilbanks, & Adams, 1979).

1.3.3 Psychogenic and social correlates

Historically, a number of psychogenic etiologies to PE have been proposed (McMahon et al., 2004), with psychiatric disorders such as anxiety and depression (Dunn, Croft, & Hackett, 1999), early hurried sexual experiences (Masters & Johnson, 1970), and psychodynamic explanations (Waldinger, 2006) having all been associated with PE in the literature. In the case of psychiatric disorders, however, there has been uncertainty with regards to the direction of causality (i.e. whether anxiety causes PE, or *vice versa*; Fasolo et al., 2005). Indeed, Rosen and Leiblum (1995) conclude that there have been attempts to establish a role for anxiety in sexual dysfunction, but that "*this research has had little direct impact on the clinical management of sexual disorders*" (p. 877). PE patients have also been shown to be significantly more preoccupied with thoughts about ejaculation control and the possibility of sexual failure compared to men who do not suffer from PE (Hartmann, Schedlowski, & Krüger, 2005). In the same study, PE patients also perceived themselves as less experienced than both their partners and men not suffering from PE, and reported lower levels of security with respect to female sexuality than controls. A link between PE and social phobia has also been described (Tignol et al., 2006), lending some additional support to a relationship between PE and anxiety states.

Socio-economic factors, such as higher level of education, occupational status (retired men are at significantly lower risk than their employed or unemployed counterparts), and having experienced a divorce have also been shown to be associated with a slightly increased risk for PE (Fasolo et al., 2005); however, direction of causality in unclear and some potential third variables could possibly explain these associations. Papaharitou and his colleagues (2006) found that the typical PE patient is relatively healthy, and likely to be single.

Studies investigating psychogenic correlates of DE are scarce. However, Cooper (1968) reported no association between general anxiety and DE, although DE patients had higher than normal scores on hostility measures. On the other hand, Munjack, Kanno and Oziel (1978) found significantly higher levels of general psychopathology in individuals with delayed ejaculation, foremostly anxiety and depression. Noting that men suffering from DE sometimes express greater satisfaction from masturbation than intercourse, and that this orientation may involve an "*idiosyncratic*

and vigorous masturbation style" (p. 647), Perelman and Rowland (2006) suggest that DE may be caused by (in addition to being secondary to potentially excessive autoerotic activity) a failure of communicating preferences for stimulation to the partner. Furthermore, they continue, some men may be less able to incite necessary arousal (i.e. by fantasizing) in the presence of a partner.

To summarize the debate on the etiology of ejaculatory dysfunction, there have been attempts to approach the etiology from several angles, both psychogenic and biogenic. However, it should be pointed out that "psychogenic" and "biogenic" etiologies are not mutually exclusive of one another – for example, many traits that are often described as "psychological" or "psychogenic" (such as anxiety, or depression) are under at least partial genetic control (e.g. Hettema, Neale, & Kendler, 2001). Gene expressions may also be the result of interactions with a particular trigger in the environment, meaning that having a certain genotype may not necessarily disrupt, for example, ejaculatory function unless some required environmental stimuli is present.

1.4 Effects of age and relationship length

The relationship between age and ejaculatory dysfunction is unclear, and vastly different and contradictory findings can be found even in the recent literature. Bancroft (1989) reported that PE generally affects younger men, and an Italian study found a significant decrease for risk of PE with age, and that PE patients were generally younger (Fasolo et al., 2005). These findings have also gained support from Papaharitou et al. (2006), who found that the typical PE patient is rather young. A large-scale survey in the US, on the other hand, found PE to be very stable across age groups (Laumann, Paik, & Rosen, 1999; Rosen, 2000), and Waldinger and his colleagues reported that median IELTs, if anything, actually seems to decrease slightly with age, suggesting an increasing risk for PE with age (Waldinger, Hengeveld, Zwinderman, & Olivier, 1998b; Waldinger, Quinn et al., 2005). However, it should be noted that there are no studies on the ejaculatory function of adolescents below 18 years of age. Most adolescents are sexually active before turning 18, and thus some potential age effects in very young men may have gone undetected. In the case of DE, there is some normal delay of ejaculatory functioning occurring during aging, however, this delay should not become exhaustive or distressing in healthy individuals (Waldinger, 2005c).

Age is naturally and quite strongly associated with relationship length, and it has been proposed that the two should be addressed together in this context (Witting et al., 2008). However, Waldinger and his colleagues (1998b) found no association

between IELT and relationship length. Finally, increasing age and relationship length both have an association with a decline in the frequency of sexual activities (Klussmann, 2002; Cristopher & Sprecher, 2000), suggesting it may be reasonable to investigate effects of frequency of sexual activity on PE and DE as well.

1.4.1 Premature ejaculation at the first sexual intercourse

Many consider the first sexual intercourse as a major changeover in life (Harvey, Flanary, & Morgan, 1986) and generally, the first sexual intercourse is an event with a stronger emotional charge than intercourses later in life (Sprecher, Barbee, & Schwartz, 1995). Little is known about whether ejaculatory dysfunctions during the first sexual intercourse differ in terms of prevalence (or any other property, for that matter) from ejaculatory dysfunction in general. A young male's first experience of intercourse is loaded with expectations and anxieties. Even though it presents an important formative experience in the sexual development of the individual, few studies have focused on the factors leading to sexual dysfunction during the first intercourse. It can be assumed that the expectations young men place on themselves with regards to their performance may be an important influence on sexual dysfunction during the first intercourse. For example, a man who subscribes to the belief that inability to achieve a firm erection, or premature ejaculation, indicates failure, may react more negatively when this actually happens compared to a man who does not subscribe to such a belief (Nobre & Pinto-Gouveia, 2006). Additionally, if anxiety is a (partially) causal factor of PE, it could be expected that PE would occur more frequently in men at their first intercourse than during later intercourses, as anxiety in relation to the first sexual intercourse experience is frequently reported by men (Sprecher, Barbee, & Schwartz, 1995).

1.5 Contextual effects and associations with different sexual activities

Little is known about contextual effects that may have an impact on ejaculatory dysfunction. In the literature, alcohol consumption has been associated with a number of sexual dysfunctions, most notably erectile dysfunction in men (e.g. Ponizovsky, 2008), but few studies have reported on the relationship between alcohol use and ejaculatory dysfunction. However, an ejaculation-delaying effect of acute alcohol intoxication has been observed (Malatesta, Pollack, Wilbanks, & Adams, 1979). Furthermore, participation in sexual activities against one's will could have an effect on ejaculatory function. In a study of young men, Boyce et al. (2006) reported that 8.7% of their participants had had sex when they had not wanted to, and 5% reported having been forced to have sex. Participation in sexual activities while not really wanting to or due to, for example, group pressure could be expected to be

associated with a less positive emotional state with an increased likelihood of sexual dysfunction.

Different sexual activities, that is, different modes of achieving ejaculation (such as through oral, vaginal, or anal sex) may also have different associations with PE, although few studies have looked into whether there is variation with regards to, for example ejaculation latency time (ELT), among different sexual activities. Waldinger (2007b) has advocated the use of activity-specific terms to describe ejaculation latency time (i.e. IELT for intra-vaginal ejaculation latency time, OELT for oral ejaculation latency time, and so forth) rather than a more global "penetration ejaculation latency time" term, suggesting there may be substantial variation in ELT between different sexual activities. Waldinger concludes that the different activities may differ from one another in "multiple technical, emotional, psychological, cultural, and religious aspects" (p. 520). Furthermore, masturbatory ejaculation latency time has been found to be predictive of IELT only in individuals not suffering from PE (i.e., masturbatory ejaculation latency time did not predice IELT in PE patients; Rowland, Strassberg, de Gouveia Brazao, & Slob, 2000). Supporting this, Corty (2008) found that the self-perceived ejaculation latency times of all partnered sexual activities (bar anal sex, which was excluded from analyses due to low frequency in the sample) were predictive of one another in a convenience sample.

1.6 Continuity of premature ejaculation

Little attention has been paid to the long-term stability of ejaculatory dysfunction, and no long-term follow-up study has been conducted on PE or DE. Some studies have, however, measured ejaculatory function over short periods of time (especially clinical drug trial studies) and reported test – re-test reliability statistics for the measures. Symonds et al. (2007) reported an intra-class correlation coefficient of .73 for test – re-test reliability on patient-reported outcomes during a four-week study with data collected on three separate occasions during this time, while Patrick et al. (2005) found intra-class correlations ranging from .63 to .87 for intra-vaginal ejaculation latency time (IELT) and patient-reported outcomes (PROs) in individuals suffering from PE and their partners over a two-week period. A Belgian study found high within-subject repeatability for ejaculation latency times with intra-class correlations ranging from .88 to .93 (Vanden Broucke et al., 2007). Althof and his colleagues (2006) found test-retest reliability correlations ranging from .70 to .90 for a questionnaire measuring sexual satisfaction, control and distress associated with PE for a period of 7-10 days. These findings indicate a substantial temporal continuity in ejaculatory dysfunction, at least over short periods of time. For long durations of time, no such statistics can be found, but stability of PE over longer time periods is

indirectly suggested by Pryor et al. (2006), whose participants reported a mean PE duration of about 16 years in a clinical drug trial study. Other studies have also implied long-term stability of PE in conducting studies on individuals suffering from "lifelong" PE (e.g. Waldinger, 2005a). Temporal stability of PE is also implied by Hawton and his colleagues (1986), who found that 75% of men who initially responded to behavioral therapy for PE did not show any lasting improvement after three years of follow-up.

2 AIMS

The general purpose of the present study was to conduct an empirical investigation of ejaculatory dysfunction in a population-based sample of Finnish men using several different indicators of ejaculatory dysfunction as measures (e.g. ejaculation latency time, subjective experience of PE or DE, and number of penile thrusts; see Grenier & Byers, 1997). There were two overall objectives. Firstly, to provide descriptive information about PE and DE. Prevalence rates of ejaculatory dysfunction in the sample were estimated, and as the literature suggests there to be uncertainty with regards to potential effects of age on ejaculatory dysfunction, age effects were examined. Next, to eludicate a potentially important factor in the etiology of PE (and possibly DE; Waldinger, Rietschel, Nöthen, Hengeveld, & Olivier, 1998) genetic and environmental influences on PE and DE were studied. Some consideration was also given to the long-term stability of ejaculatory dysfunction, and whether and to what extent such stability is explained by genetic or environmental factors. Secondly, we aimed at providing some insights regarding the formulation of diagnostic criteria for PE and DE. To get an overview of the impact ejaculatory dysfunction may have on individual well-being, the relationship between ejaculatory dysfunction and personal sexual distress was assessed, and different PE indicator variables were examined to investigate if some threshold of experiencing substantial distress could be identified. Finally, a number of factors that could affect, or potentially distort measurements of, ejaculation latency times were assessed.

The specific research questions were as follows:

1. What is the prevalence rate of PE and DE in a Finnish sample? (Studies I-III)
2. How are age and relationship length associated with PE and DE? (Studies I-VI)
3. How is sexual orientation associated with PE and DE?
4. Is there an association between experiencing PE during the first intercourse and suffering from PE later in life? (Study IV)
5. Are there genetic effects on PE and DE, and if so, how large a proportion of the total variance in PE or DE is under genetic influence? (Studies I-IV)
6. Is there anything to suggest that PE is a stable condition over time, and if so, is such stability caused by genetic or environmental influences? (Study IV)
7. Are contextual factors affecting PE during the first intercourse? (Study VI)
8. Is PE, or any specific indicator of PE, associated with sexual distress, and if so, are there measurable thresholds related to ejaculatory functioning where sexual distress becomes more prominent? (Study V)

9. What are the unique associations of age and relationship length (i.e. of age when relationship length is controlled for, and vice versa) with ejaculation latency time? (Study VI)
10. Is there an association between ejaculation latency time and frequency of engaging in different sexual activities (e.g. vaginal, anal or oral sex)? (Study VI)
11. Is there an association between ejaculation latency time and achieving ejaculation through different modes (e.g. through vaginal, anal or oral sex)? (Study VI)

3 MATERIALS AND METHODS

3.1 Participants

The present study was a part of the "Genetics of Sexuality and Aggression Study", a large project conducted at the Center of Excellence in Behavior Genetics at Åbo Akademi University. The participants were a subset from the Genetics of Sexuality and Aggression (GSA) sample, which also includes women. The main GSA sample consists of two data collections: The first one was carried out in 2005 and targeted 33-43-year-old twins. Questionnaires, followed by a reminder letter and later a new questionnaire were sent to a total of 10,000 individuals, half of which were men (twin pairs were sampled according to their dates of birth from the above mentioned date backwards until 2,000 male-male, 2,000 female-female and 1,000 opposite-sex twin pairs had been identified). The questionnaires were finally returned by 1,313 (27%) men; the overall response rate of the study, including women, was 36%.

The second data collection was carried out in 2006 (there was no overlap between the data collections) and targeted 18-33-year-old twins and their siblings aged 18 or above. A total of 23,577 individuals, of which 11,914 were men, were contacted by post and asked if they would be interested in completing a sexuality-related questionnaire. Participants who did consent to participate were given the option of completing the questionnaire by mail, or online through a secure internet web page. Next, the questionnaires were sent, followed by a reminder letter. A total of 3,923 men (33.9%), of which 2,660 (33.7%) were twins and 1,263 (31.5%) were siblings of twins responded to the survey. With both data collections combined, a grand total of 5,236 participants (30.8%) was achieved. Including female participants, this study had an overall response rate of 44.6% All participants in both data collections were identified from the Finnish Central Population Registry. Furthermore, all were native Finnish speakers. The questionnaires were extensive and covered a wide array of sexual behavior and attitudes, childhood experiences, aggression, and alcohol use. The purpose of the study was clearly described and the voluntary and anonymous nature of the participation emphasized.

Study II was based on the first data collection, studies I and IV were based on the second data collection, and studies III and V-VI on both data collections (Table 1). However, there was some discrepancy between the data collections with regards to what instruments were included; hence some individual statistical analyses in the latter three studies may have been conducted on data from only one data collection. Furthermore, as can be seen in Table 1, there is some overlap between studies with regards to the study populations (e.g. the entire study population of Study II

constitutes a subpopulation of Study III), which has implications for the comparison of the different studies, as they are naturally correlated.

Table 1
An Overview of Research Questions, Data Collections and Participants in the Original Studies.

Study	Study queries	Data collection	Participants (*N*)	Age of participants
I	Prevalence of PE at the first sexual intercourse Contextual effects on PE at the first sexual intercourse Genetic and environmental influences on PE at the first sexual intercourse Effects of age of first intercourse participation on PE	II	3,186 individuals 2,230 twins 678 MZ individuals 1,471 DZ individuals 81 undetermined 956 siblings	18-48
II	Genetic and environmental influences on PE and DE Prevalence of PE and DE Age effects	I	1,273 twin individuals 389 MZ individuals 807 DZ individuals 77 undetermined	33-43
III	Genetic and environmental influences on PE and DE Prevalence of PE and DE Age effects	I + II	3,946 individuals 3,094 twins 933 MZ individuals 1,004 DZ individuals 136 undetermined 852 siblings	18-48
IV	Stability of PE and DE over time Genetic and environmental influences on the stability of PE and DE over time Effects of time passed between first intercourse and time of study participation	II	2,633 individuals 1,812 twins 536 MZ individuals 1,183 DZ individuals 93 undetermined 821 siblings	18-48
V	Relationship between different PE indicator variables and sexual distress Age effects on different PE indicator variables	II	3,332 individuals 2,328 twins 1,004 siblings	18-48
VI	Effects of age and relationship length on ELT Effects of frequency of different sexual activities on ELT Effects of different modes of achieving ejaculation on ELT	I + II	3,997 individuals 3,134 twins 863 siblings	18-48

Note. Discrepancies in the number of participants between studies conducted on data from the same data collection, or on overlapping samples, are due to discrepancies between response rates to individual instruments.
PE = premature ejaculation, DE = delayed ejaculation, ELT = ejaculation latency time, MZ = monozygotic twin, DZ = dizygotic twin.

To avoid heterosexist bias and improve generalizability of the results, individuals with homosexual experience have not been separated from exclusively heterosexual individuals in any of the six studies (except when reporting frequency of engaging in anal sex in Study VI), although effects of sexual orientation have been controlled for in several instances (as noted in the respective studies). However, as there is some uncertainty regarding relationship between ejaculatory dysfunction and sexual orientation, additional analyses were conducted specifically for this thesis to examine how sexual orientation is associated with ejaculatory dysfunction (either directly, or through moderation of frequency and type of different sexual activities). These analyses are described in the final paragraph of section 4.3.

3.2 Measurements

The main measures used in the present study will be described briefly below. For more thorough descriptions of the measures, the reader is advised to consult the original publications.

3.2.1 Measurement of premature ejaculation during the first intercourse (Study I and IV)

This instrument was created specifically for the present study. The participants indicated the extent to which the following items were true concerning their first intercourse experience: ejaculation prior to penetration, ejaculation almost immediately after penetration (1-3 penetrations), ejaculation in less than 1 minute after penetration, and fear of premature ejaculation. A composite variable (ranging from 0-4) was then formed of these four variables, with higher values indicating more problems related to PE. This composite variable was subsequently divided by the number of variables (i.e. 4), in order to achieve a variable on a scale from 0-1.

3.2.2 Measurement of current premature and delayed ejaculation (Studies II-VI)

Ten questions were used to tap both objective and subjective aspects of ejaculatory function. The questions were designed to take different definitional aspects into account: number of penile thrusts, ejaculation latency time, ejaculation prior to intercourse (*ante portas*), subjective experience of PE, pretending to ejaculate, later ejaculation than desired, trying to speed up intercourse, trying to delay intercourse, worrying about ejaculation, and feeling of control over ejaculation. To avoid heterosexist bias and exclusion of both female–male and male–male anal intercourse, we used a gender neutral definition of ejaculation latency time inclusive of anal

intercourse. The questions were adapted from an unpublished questionnaire developed by Grenier and Byers (1997). At the time when this study was conceived and executed, there were no validated questionnaire measures of PE available. These variables were subjected to factor analyses, based on which composite variables measuring PE and DE were created, with higher values on either variable indicating more problems related to PE, or DE. The items 1) *subjective experience of PE*, 2) *worrying about ejaculation*, 3) *feeling of control over ejaculation*, 4) *ejaculation prior to intercourse*, 5) *number of penile thrusts*, 6) *ejaculation latency time*, and 7) *tried to slow down intercourse* constituted the PE composite variable, However, item 7 had complex loadings and was included in the DE composite variable in Study II. Confirmatory factor analyses on the substantially larger sample of Study III indicated that it was, in fact, better suited for the PE factor and was thus subsequently included in that factor. The items 8) *pretending to ejaculate*, 9) *later ejaculation than desired*, 10) *tried to speed up intercourse* constituted the DE composite variable; with the addition of item 7 in Study II. Descriptive statistics and frequency distributions for the response alternatives of these variables can be seen in Table 1 of both Study II and IV (note that the participants were from different data collections in these studies). Note that there is overlap between studies with regards to the sample (for example, the participants in Study II are a subpopulation of the total study population in Study III), explaining similarities of the results between studies.

3.2.3 Sexual Distress Scale (Study V)

The instrument measuring sexual distress was developed from the Female Sexual Distress Scale (FSDS; Derogatis, Rosen, Leiblum, Burnett, & Heiman, 2002). Originally a 20-item questionnaire intended for females, the FSDS includes gender neutral questions of which seven were chosen to measure sexual distress in the present sample. The questions were on a Likert-type scale ranging from 0–4 (0 = never, 1 = rarely, 2 = occasionally, 3 = frequently, 4 = Always; see Appendix). The questions were back translated into Finnish. Although not validated in a male sample, the FSDS has been shown to have good reliability and validity in previous studies with female samples. Additional analyses to ensure suitability of the instrument also in the male setting were conducted and reported. The variables were subject to factor analysis. All items loaded well on one factor, and subsequently a composite variable measuring sexual distress was formed, with higher values indicating more sexual distress. The variables constituting this composite variable had excellent internal consistency (Cronbach's α = .892).

3.2.4 Desired and Actual Sexual Activity Scale (Study VI)

Frequency and variation in sexual activity was measured using a modified version of Section III from the Derogatis Sexual Functioning Inventory (DSFI; Derogatis, 1975; Derogatis & Melisaratos, 1975), referred to here as the Desired and Actual Sexual Activity Scale (DASA; Santtila et al., 2008). The original version of the DSFI consists of the items "sexual fantasies", "kissing and petting", "masturbation", and "intercourse". In the DASA, the following changes were made to the items in the DSFI: 1) the item "intercourse" was divided into "vaginal intercourse" and "anal intercourse"; 2) the item "oral sex" was added to the inventory; and 3) the item "masturbation" was specified as solo masturbation. Individuals were asked how frequently they engaged in each type of behavior using a nine-point scale, where 0 indicating no engagement, and 8 indicated "at least four times a day". Only variables measuring actual sexual activity were selected for analyses; namely frequency of oral, vaginal and anal sex, and masturbation.

3.2.5 Modes of Ejaculation (Study VI)

In order to investigate how ejaculation had been achieved (namely; by different types of partnered sexual activities), one item was created specifically for this study. This item was formulated as "In the last two years, how have you achieved ejaculation in sexual interplay with a partner?", with the corresponding response alternatives of "through manual stimulation by the partner", "through oral sex", "through vaginal sex", and "through anal sex". The participants could select several of the response alternatives as appropriate. For all analyses, this item was treated as four separate dichotomous variables (e.g. "through vaginal sex" with response alternatives yes and no).

3.3 The twin design

There are two basic approaches to investigating the biological basis of a trait: quantitative genetics, and molecular genetics. In quantitative genetics, adoption studies and the twin (or family) design are the available study methods. In the present study, only the quantitative genetic approach was used. The twin design is based on the difference in genetic relatedness between monozygotic (MZ) and dizygotic (DZ) twins. MZ twins have their complete genetic makeup (i.e. 100%) in common, whereas DZ twins (on average) share half (50%) of theirs. Thus, if a trait is heritable, MZ twins will be more similar to each other on that particular trait compared to DZ twins. This assumes validity of the so-called "equal environments assumption", which states that both twins share equally correlated environments of

etiological importance for a trait. The equal environments assumption has been rather extensively tested and appears to be valid for most traits (Bouchard & Propping, 1993). Using the twin design, one can decompose individual differences in behavioral phenotypes (such as sexual behavior) into genetic and environmental effects. Genetic influences may further be divided into additive *(A)* and non-additive *(D)* genetic influences, while environmental influences may be divided into shared *(C)* and non-shared *(E)* components. The non-shared environmental component *E* is also inclusive of measurement error. The additive genetic influence refers to the total effect of multiple alleles on the phenotype, while non-additive genetic influence refers to the interactive effect among multiple alleles (i.e. dominance) and multiple genes (i.e. gene-gene interaction or *epistasis)* on the phenotype. By definition, shared environmental influences are any non-genetic influences that contribute to familial resemblance among relatives, and non-shared environmental influences are factors whose influence is unique for each individual.

The overlap and independence of different sexual behavior variables can also be examined using bi- or multivariate quantitative genetic designs that estimate the extent to which the same genetic (or environmental) effects underlie the covariance between two (or more) phenotypic traits (Plomin, DeFries, McClearn, & McGuffin, 2001). The classical twin design includes twins only, but an extended design including siblings of twins increases statistical power, especially for detecting non-additive genetic or shared environmental influences (Posthuma & Boomsma, 2000). Furthermore, quantitative genetic research provides a foundation for molecular genetic studies that aim to chart the specific genes that are causal of the observed genetic effects.

3.4 Zygosity determination

Zygosity of the twins was determined with the aid of three questionnaire items (Sarna, Kaprio, Sistonen, & Koskenvuo, 1978). These items have been shown to be 95% accurate in zygosity determination compared with blood typing analyses (Eisen, Neuman, Goldberg, Rice, & True, 1989).

3.5 Statistical analyses

The basic statistical analyses, including exploratory factor analyses (EFA), were conducted using SPSS 14.0 and 15.0. Confirmatory factor analyses (CFA) were conducted using AMOS Graphics 5.0.1. Due to the fairly large sample size in the present group of studies, and given the potential limitations of the χ^2 test, we chose to report and consider five additional measures of model fit for the CFA: either the

normed-fit index *(NFI)* or the Tucker-Lewis index *(TLI)*, the goodness-of-fit index *(GFI)*, the root-mean-square error of approximation *(RMSEA)* and its adjacent null hypothesis test *(PCLOSE)*, the Akaike information criterion *(AIC)*, and finally, Hoelter's "critical *N*". The fit of the model was considered to be supported if the *NFI* was greater than .95 (Thompson, 2004), if *GFI* was greater than .90 (Arbuckle & Wothke, 1999), if the *RMSEA* was roughly equal to, but preferably less than, .06 (Thompson, 2004), and Hoelter's "critical *N*" greater than 200. The *AIC* was used for comparing models, with a lower value indicating better fit. In order to avoid dependence, members of a twin pair were included in separate factor analyses, or only one randomly chosen member of a family was included.

For phenotypic analyses, the Complex Samples procedure of SPSS was used. This procedure allows the data to be correlated and adjusts the estimates of standard errors, thus allowing inclusion of members from the same family simultaneously. The statistical tests used were general linear model, multiple regression and simple contrasts. The Mx statistical package (Neale, Boker, Xie, & Maes, 2003) was also used for analysis of means and variances, as well as twin (phenotypic) correlations.

Genetic analyses were conducting exclusively using Mx, a statistical package designed for twin and sibling analyses (Neale et al., 2003). When conducting genetic analyses, models are tested that decompose observed (i.e. phenotypic) variation in a variable into additive genetic influences *(A)*, shared environmental influences *(C)*, and non-shared environmental influences *(E)*, the latter also inclusive of measurement error (i.e. $Vp = A + C + E$). In addition, non-additive genetic influences *(D)* may also contribute to the phenotypic variance, but *D* cannot be estimated simultaneously with *C* with twin data only. MZ correlations that greatly exceed twice the corresponding DZ correlations imply that dominance effects may be present for the given phenotype. No *D* models were suitable for the data in the present study, and thus no further attention will be paid to the *D* parameter.

In Studies I-III, univariate models were fitted to the data, and in Study IV, a bivariate correlated factors model was tested. Raw, age-regressed variables were used in all model-fitting scripts using Mx with maximum likelihood estimation. This method allows inclusion of singletons (i.e. when data is available only for one twin of a twin pair), as well as siblings of twins, thereby increasing the statistical power of the analysis. To determine the impact of a parameter (i.e. *A, C,* or *E*), simpler, or *nested* models were tested against the full *ACE* model. A non-significant decrease in the -2 x log-likelihood of data indicates that the nested model (i.e. with fewer parameters) provides a reliable, but more parsimonious, fit to the data compared with the full model (i.e. an *AE* model may be more parsimonious than the full *ACE* model, meaning that the effects of the shared environmental parameter are negligible, and

that the *C* parameter should be omitted). The subtraction gives a χ^2 value and associated degrees of freedom which can be tested for significance. A non-significant χ^2 value indicates that the more parsimonious model does not have a significantly worse fit than the full model, and should thus be accepted. In addition, the *AIC* (*AIC* = χ^2 - 2 x degrees of freedom) was considered. A lower value indicates a better fit of the model to the observed data (Akaike, 1987).

Genetic and environmental effects on the continuity (of PE) were estimated by inserting variables measuring PE during the first intercourse, and PE at present into a bivariate correlated factors *ACE* model. In this model, genetic and environmental correlations are estimated, revealing to what extent the same genetic (or environmental) factors are causing the variance in the observed phenotypes.

Two separate analyses (i.e. that were not included in any of the six publications), were conducted as well. First, an analysis to determine whether age moderates the association between sexual distress and ejaculatory latency time was performed. We were interested in investigating whether there is a tendency to "come to terms" with a short ejaculation latency time with age. To accomplish this, the participants of Study V (n = 3,332) were categorized into two groups based on the median age of the sample (which was 27 years). Correlations between the variables measuring ejaculation latency time and sexual distress were then compared between these two groups. Next, in order to determine whether the difference between the correlations was statistically significant, an interaction term was computed first by centralizing the variables measuring age and ejaculation latency time (by subtracting the means from both). The centralized variables were then multiplied to form the interaction term. This variable was then inserted as a covariate in a Complex Samples General Linear Model regression together with the variables measuring age and ejaculation latency time. The composite variable measuring sexual distress was inserted as the dependent variable. The results of this analysis are presented in section 4.2.

Second, to investigate the association between sexual orientation and ejaculatory dysfunction, the item measuring any same-sex sexual behavior (Have you ever engaged in sexual activity with another man?) was used to predict PE and DE using the Generalized Estimating Equations module of SPSS 16.0. This procedure takes dependence between participants into account. Age was used as a covariate in all analyses. As there may be differences in frequency and type of sexual activities between exclusively heterosexual individuals and individuals with at least some homosexual experience, we decided to control for effects of frequencies of different sexual activities (see section 3.2.4), as well as different modes of achieving ejaculation (see section 3.2.5). Data for these analyses were available from 3,103 participants (all from the second data collection). For the items measuring ejaculatory function,

missing values were imputed for all participants with at least one response (out of 10), that is, data were imputed using intra-scale information. The results of this analysis are presented in section 4.3.

4 RESULTS

4.1 Prevalence of indicators of premature and delayed ejaculation (Studies I-III)

As outlined in the introduction, the prevalence of PE or DE will differ drastically depending on choice of definitional criteria. Therefore, prevalence figures will be presented as follows: firstly, in terms of subjective reports (and in the case of Study I, fear of premature ejaculation) of PE or DE; and secondly, on the basis of a (self-reported) ejaculation latency time of less than 1 minute, or the participant declaring himself not usually being able to achieve ejaculation at all (the latter not available for Study I). Thirdly, the frequency with which anteportal ejaculation occurs in the sample will be reported. Additional statistics relevant to the prevalence figures are also presented. For the first intercourse experiences, DE was not measured.

4.1.1 Premature ejaculation during the first intercourse (Study I)

Study I concentrated on PE during only the first sexual intercourse (DE was not investigated in this study). 45.8% reported experiencing fear of PE in relation to the first intercourse. An IELT of less than 1 minute was reported by 29.5%, an exceptionally large figure compared to population studies not focused on the first intercourse. An additional 3.7% reported ejaculation *ante portas*. For comparison, 11.8% reported ejaculating within 1-3 penile thrusts. The composite variable measuring PE during the first intercourse (PE-1st) had, given the low number of variables constituting it, reasonable internal reliability (Cronbach's α = .45). PE-1st was then divided by the number of variables constituting it, thus converting it to a scale ranging from 0-1 (the composite score constituted of four dichotomous variables where participants were asked to indicate whether they agreed with a statement or not) and had the following properties: M = 0.23, SD = 0.24. In other words, participants on average agreed to a proportion of 23% of the variables measuring PE during the first intercourse.

4.1.2 Current premature ejaculation (Studies II, III and V)

In Study II, which consisted of data from the first data collection (and thus, men aged 33-43 years, M = 37.56, SD = 3.21) 3.6% of the participants indicated that they "always or nearly always" ejaculated too early, while an additional 37.9% felt they "usually" ejaculate too early. An inter-study comparison of five different indicators of PE and DE can be seen in Table 2. In Study II, 1.8% reported ejaculating within 1

minute of vaginal or anal penetration; however, 9.2% reported managing only 10 penile thrusts or less. Study V consisted of data from the second data collection (with men aged 18-48 years, $M = 26.17$, $SD = 4.77$) only. The findings of this study were much in line with those of Study II, with 3.1% of the participants indicating that they "always or nearly always" ejaculated too early (35.5% felt they "usually" experienced PE), and 1.9% reporting an ejaculation latency time of less than a minute. Also in Study II, 1.6% reported ejaculating anteportally in more than 50% of intercourses (0.5% reported "always or almost always" suffering from anteportal ejaculation). 73.8% reported that anteportal ejaculation occurred "never or very rarely". In study IV, which had no sample overlap with study II, somewhat fewer participants reported anteportal ejaculation in more than 50% of intercourses (1%; and 0.3% did so "always or almost always"). The number of participants reporting "never or very rarely" suffering from anteportal ejaculation was also considerably higher at 85.3%. In study II, again, 5.4% reported managing only 10 penile thrusts or less. Study III was conducted with data from both collections (participants were aged 18-48 years, $M = 29.91$, $SD = 6.91$), and results were, predictably, quite closely reflecting the findings of studies II and V. The results are consistent with previous research findings (e.g. Montorsi, 2005; Waldinger, 2005d). When the different indicator variables of PE (e.g. ejaculation latency time, number of penile thrusts, and subjective experience; see Table I of Study V) were assessed individually, the variable measuring subjective experience of PE had the strongest correlations with other PE indicator variables. Between all variables, correlations ranged from an insignificant zero to $r = .45$ ($p < .001$).

4.1.3 Current delayed ejaculation (Studies II, III and V)

As can be seen in Table 2, positive indicators of DE (the last two rows) appears to be rare, with frequencies ranging from 0.2-2.6% between the two indicators, and generally less prevalent than positive indicators of PE (rows 1-3), also confirming the results of previous studies (e.g. Jannini & Lenzi, 2005; Perelman & Rowland, 2006). Interestingly, positive indicators of DE seem to be more prevalent in the sample including adolescents and younger men (Studies V and III), however, while the mean age of this sample is younger, this sample is also inclusive of the oldest participants of the present group of studies (i.e. siblings of twins up to 48 years old).

Table 2
Comparison of Prevalence Figures between Studies for Indicators of Current Premature and Delayed Ejaculation.

Indicator variable	Study II (Data collection I)	Study III (Data collection I+II)	Study V† (Data collection II)
Always or nearly always ejaculating too early [1]	3.6%	3.1%	3.1%
Anteportal ejaculation in more than 50% of intercourses [1]	1.6%	1.2%	1.0%
Ejaculation in less than 1 minute from penetration [1]	1.8%	1.8%	1.9%
Able to decide when to ejaculate "always or "nearly always"	10.4%	8.6%	7.9%
Usually does not ejaculate during intercourse [2]	0.4%	1.9%	2.6%
Does never ejaculate during intercourse [2]	0.2%	1.1%	1.4%

Note. † = Studies IV and V were conducted on the same data collection. Prevalence rates may be slightly discrepant between the studies, occasionally also between studies conducted on samples from the same data collection. This discrepancy is as a result of using samples from different data collections in different studies, or fluctuation in response rates to different instruments.
[1] = variable indicates premature ejaculation
[2] = variable indicates delayed ejaculation

4.2 Effects of age on premature and delayed ejaculation (Studies I-VI)

Study I focused only on the first intercourse experience. The age at which the individual had participated in the first intercourse (i.e. the timing of the intercourse) was not related to PE. However, as reported in Study IV, age at the first intercourse did have (weak) positive associations with both current PE ($r = .050$, $p < .05$; $R^2 = .003$; $F = 7.488$, $t = 2.736$, $p < .006$) and current DE ($r = .063$, $p < .01$; $R^2 = .006$; $F = 11.047$, $t = 3.324$, $p < .001$) later in life, indicating that problems related to both PE and DE tend to increase slightly with increasing age. On a side note, age at the first intercourse was also positively associated with current age ($r = .172$, $p < .001$), probably reflecting a cohort effect on age of sexual debut.

Studies II-VI were, on the other hand, focused on the effects of the age of the participants when they participated in the survey on their reports of current premature and delayed ejaculation. Generally, effects of age were negligible or very weak. In Study II, which was conducted on a quite homogenous sample in terms of age (33-43-year-olds), no significant effects of age were detected. In Study III, which

had a larger and, in terms of age, broader sample (18-48-year-olds), significant but small effects of age were detected for PE, so that problems related to PE increased with age. No significant association between DE and age could be established. As can be seen in Study V, some PE indicator variables also had, relatively speaking, stronger associations with age than other indicators comprising the composite variable, with the strongest associations detected for variables measuring ejaculation latency time (which is elaborated separately in section 4.5.1) and feeling of control over ejaculation ($r = .08$, $p < .01$; $F = 26.143$, $t = 5.113$ [both $p < .001$]; $R^2 = .007$). The same pattern with negligible to weak effects of age is repeated through studies IV-VI. The associations of individual PE indicators with age indicate increasing PE problems with increasing age with the exception of variables measuring perception of control over ejaculation, and worrying about ejaculating too early. Indicator variables indicative of DE were not significantly correlated with age. Composite variables measuring PE were always positively associated with age, that is, the problems increased with increasing age. However, as can be seen in Table 3 of Study V, the associations of individual PE indicator variables were barely detectable with only four out of ten reaching statistical significance. Relative to all the other different PE indicator variables in Study V, the variables measuring number of penile thrusts, and ejaculation latency time had the strongest association with age.

Next, we attempted to assess whether age moderates the relationship between sexual distress and ejaculation latency time. This analysis was conducted outside the scope of the six papers. The participants of Study V were categorized into two groups based on median age (27 years). The correlation between ejaculation latency time and sexual distress for those of comparatively higher age ($r = -.069$, $p < .05$) was very similar to the same correlation in those of comparatively younger age ($r = -.099$, $p < .05$). Next, the composite variable measuring sexual distress was inserted as the dependent variable in a CSGLM regression, with the age interaction term and variables measuring age and ejaculation latency time as covariates. No significant interactive effect between age and ejaculation latency time was detected, indicating that the association between ejaculation latency time and sexual distress was stable over time. In addition, as the correlations of ejaculation latency time and sexual distress were overall low, it seems that ejaculation latency time has a quite negligible relationship with sexual distress.

4.3 Effects of sexual orientation on premature and delayed ejaculation

No significant association between sexual orientation and PE was detected ($p = .680$), but individuals who had had a homosexual experience had significantly elevated levels of DE ($M = 1.303$, $SE = 0.044$) compared to those who had no such experience ($M = 1.153$, $SE = 0.009$; $B = 0.151$, $SE = 0.045$, $\chi^2(1) = 11.377$, $p < .001$).

Next, we investigated the effect of sexual orientation on the four variables measuring different modes of ejaculation and the four variables measuring frequency of different sexual activities. As can be seen in Table 3, the frequencies for all modes of achieving ejaculation differed significantly between exclusively heterosexual participants and participants who had engaged in homosexual behavior, so that the latter were more likely to have achieved ejaculation by all modes except vaginal sex. Individuals with homosexual experience also engaged significantly more frequently in all sexual activities except vaginal sex.

Table 3
Effects of Sexual Orientation on Variables Measuring Modes of Ejaculation and Frequency of Different Sexual Activities.

		Homosexual Behavior		
		B	*SE*	χ^2
Modes of Ejaculation				
	Manual stimulation by partner	0.537	0.147	13.393**
	Oral sex	0.422	0.140	9.047**
	Vaginal sex	-2.933	0.219	179.429***
	Anal sex	1.408	0.139	102.135***
Frequency of Sexual Activities				
	Masturbation	0.942	0.103	84.512***
	Oral sex	0.430	0.105	16.794***
	Vaginal sex	-0.559	0.124	20.195***
	Anal sex	0.524	0.073	51.965***

Note. SE = standard error, df = 1 for all analyses. A positive *B*-value indicates a positive association with having ever engaged in sexual activity with another man.
** = significant on the $p < .01$ level
*** = significant on the $p < .001$ level

Finally, to investigate whether the effect of sexual orientation on DE was direct, or indirect (through mediation of differences in modes and frequency of different sexual activities), the effect of sexual orientation on DE was re-calculated controlling for effects of frequency of sexual activities and modes of ejaculation. When these effects were controlled for, there was no remaining significant effect of sexual orientation on DE ($p = .884$). In summary, there does not appear to be any direct effects of sexual orientation on ejaculatory dysfunction, but sexual orientation may affect ejaculatory function indirectly through differences in types and frequency of sexual activity.

4.4 Associations between premature ejaculation at the first sexual intercourse and current premature and delayed ejaculation (Study IV)

Participants who had reported PE during the first intercourse were significantly more likely to report PE symptoms at present. Participants for whom a relatively short period of time had passed between the first intercourse and the present reported higher stability in PE compared to those with a relatively long time difference (r = .403 and r = .340 for the two groups, respectively, both $p < .001$). Having reported PE during the first intercourse was also significantly associated with reporting DE later in life, this association being of course negative (r = -.213 for the group with a relatively short age difference between first intercourse and present, r = -.163 for the group with a relatively long age difference between first intercourse and present, both $p < .001$). The difference in stability of PE was not significant between the two groups, however, for DE a significant interaction term (F = 5.214, t = 2.283, $p < .05$) was observed, indicating that the difference between the correlations between PE during the first intercourse and current DE was significant (i.e., the strength of the association were significantly different between the two groups). In order to get an overall picture of the strength of the continuity in PE, current PE was predicted by PE during the first intercourse, time difference between the first intercourse and present, and the age interaction term. Quite strong associations with current PE were detected (R^2 = .145 for the full model); with PE during the first intercourse contributing the lion's share of the variance (F = 298.829, t = 17.287, $p <$ .001).

4.5 Genetic and environmental influences on premature and delayed ejaculation (Studies I-IV)

The first step in determining the genetic effects on a trait is to compute twin, or family, correlations. In other words, correlations for a trait are computed firstly between MZ twins (i.e. a brother pair), and these correlations are then compared to the corresponding correlations of DZ twins, or indeed any other combination of same-sex siblings excluding MZ twins. The rationale here is that all same-sex sibling constellations bar MZ twins have a genetic resemblance of around 50%, and thus any such same-sex biological sibling pair may be treated as a DZ twin pair in statistical analyses given that no differences between DZ twin pairs and other sibling pairs are detected. There are two potential differences that may bias the results. Firstly, there may be differences in correlation sizes between DZ twins and other sibling constellations in which the siblings have a genetic resemblance of 50%. Such differences could arise as a product of twin-specific environments (e.g. prenatal effects from sharing the womb, or parents and teachers treating twins more similarly

than other kinds of siblings and thus leading to increased resemblance between DZ twins compared to non-twin sibling pairs). Detection of such effects would jeopardize valid estimation of genetic effects. In the present group of studies, we have partly controlled for such effects by equalizing correlations between all sibling constellations except MZ twins. No significant differences in correlations between the above mentioned sibling constellations (including DZ twins) were detected. Secondly, if there are intra-variable differences between twins and non-twins (i.e. differences in the level of a variable; that either twins or non-twins score significantly higher on a given variable), generalizability of, for example, prevalence estimates made on a twin sample could be in jeopardy. In other words, such differences would suggest that twins differ qualitatively from other people with regards to a particular trait. In the present study, no such level differences were detected. Differences could theoretically also stem from cohort effects, because twins are born at the same time whereas other siblings are not. Correlations (from Study IV) for current PE and DE, as well as for PE during the first intercourse (from Study I) are presented in Table 4. Next, structural equation modeling scripts are applied to the data in order to determine the size and statistical significance of genetic and environmental effects. The results of the genetic analyses are presented in this pattern below.

Table 4
Family Correlations (with 95% Confidence Intervals) for Premature and Delayed Ejaculation.

	Current PE	Current DE	PE-1st
r_g = 1.00	.305 (.169 - .423)	-.001 (-.171 - .170)	.300 (.145 - .431)
r_g = .50	.130 (.031 - .227)	.088 (-.004 - .180)	.101 (.005 - .197)

Note. PE = premature ejaculation, DE = delayed ejaculation, PE-1st = PE at the first sexual intercourse.
r_g = 1.00 refers to monozygotic twin pairs.
r_g = .50 refers to any kind of sibling pair except monozygotic twins pairs (i.e., siblings that share about 50% of their genes).

4.5.1 Premature ejaculation during the first intercourse (Studies I and IV)

As seen in Table 4, phenotypic correlations indicated presence of genetic effects on PE during the first intercourse. In Study I, the univariate *ACE* model fitting results revealed significant genetic effects of around 22%, and the rest of the variance was accounted for by non-shared environmental effects. Shared environmental effects were estimated to zero in the full model, and omission of the shared environmental parameter *C* did not significantly reduce the fit of the model, hence an *AE* model was selected. This was true in Study IV as well, although the parameter estimates revealed a slightly stronger genetic effect this time, with additive genetic effects accounting for 28% of the variance and the rest being due to *E* effects. Fluctuations in

heritability estimates are partly due to variations in sample populations (and size) between studies. In addition, a bivariate model will have higher statistical power, which may also partly explain the somewhat larger estimate reported in Study IV. An overview of the heritability estimates in the studies can be seen in Table 5. Some contextual effects were also found to affect PE during the first intercourse, namely having sex with an unknown partner, and alcohol or drug intoxication, which both decreased the likelihood of suffering from PE during the first intercourse. Alcohol use and having sex with an unknown partner were related to decreases in positive affect, and both positive and negative affect were related to a higher likelihood of PE during the first intercourse (Study I). Contextual effects such as these may contribute to the non-shared environmental variation, which constituted the majority of the phenotypic variation, in PE during the first intercourse.

4.5.2 Current premature ejaculation (Studies II-IV)

Family correlations for the composite variable measuring PE were very similar between studies. Intra-class correlations for MZ twins amounted to $r = .30$ in all three studies (II-IV), and for other sibling pair types ranged from ($r = .13$) in studies III and IV to ($r = .15$) in Study II. However, the study populations were (at least partly) overlapping between studies, and this naturally contributes to making the results more uniform. These correlations are all indicative of genetic influence on PE. Univariate model fitting results confirmed this pattern, with additive genetic effects estimated at 28% in both studies II and III, with 72% of the variance accounted for by non-shared environmental effects (Table 5). Again, the shared environmental component could be dropped without significant reduction of model fit and an *AE* model was best fitting for the data. In Study II, which had a substantially smaller sample than Study III, model fit did not drop significantly when omitting the additive genetic component *A* either, but both *A* and *C* could not be dropped simultaneously. In other words, a significant familial effect was detected, but (probably due to insufficient statistical power) although most indicators pointed towards the effect being genetic, this could not be conclusively proven. In Study III, however, the *A* component reached significance. Study IV tested a bivariate solution, replicating the finding of Study III, with a genetic effect accounting for 31.5% of the variance this time. Also in line with the previous study, the influence of the *C* component was not significant (i.e. non-shared environmental effects accounted for 68.5% of the variance).

4.5.3 Current delayed ejaculation (Studies II-IV)

As can be seen in Table 4, there was no reason to expect any significant genetic effects on DE based on the family correlations. This pattern of similar correlations between MZ twins and other sibling pair types was continued in studies II and III, albeit with slightly higher overall correlations in Study II (r_{mz} = .20; r_{dz} = .23). Study III, had correlations around zero for both. *ACE* model fitting analyses in Study II, however, did find a significant familial effect, with the full model suggesting that shared environmental effects accounted for 24% of the variance (Table 5).

Table 5
Comparisons between Studies of Heritability Estimates for Premature and Delayed Ejaculation with Descriptions of Best Fitting Models.

Study	*Estimates of Variance Components (Full Model)*						*Best fitting model*	
	A_{PE}	C_{PE}	E_{PE}	A_{DE}	C_{DE}	E_{DE}	PE	DE
Study II	.28	.00	.72	.00	.24	.76	*AE*[1]	*CE*
Study III	.28*	.00	.72	.00	.07	.93	*AE**	*AE*
Study IV [a]	.28*	.00	.72	*n/a*	*n/a*	*n/a*	*AE**	*n/a*
Study IV [b]	.32*	.00	.68	.05	.00	.95	*AE**	*AE*[1]

Note. *A* = additive genetic effects, *C* = shared environmental effects, *E* = non-shared environmental effects, PE = premature ejaculation, DE = delayed ejaculation. The non-shared environmental component (*E*) contains error variance. There was no overlap between the samples of Studies II and IV, but both these samples were combined to form the study population of Study III.
* = significant on the $p < .05$ level
[a] = premature ejaculation during the first intercourse
[b] = premature ejaculation at the time of study participation
[1] = significant familial effect (i.e. cannot be concluded whether effect is attributable to *A* or *C*)

The *A* component was estimated to zero in the full model, and thus 76% of the variance was accounted for by non-shared environmental effects. Testing of different nested models revealed that model fit was not significantly reduced when dropping either the *A* or the *C* component individually. Again, however, both could not be simultaneously omitted, suggesting a significant familial component with indications that the familial effect would be accounted for by *C* effects. The pattern was similar in Study IV, in which the full model instead suggested a weak genetic effect (of around 5%), but again, both the *A* and the *C* could be dropped without reduction of model fit, as long as they were not done so simultaneously. However, in Study III, which had the largest sample of these studies, the full model yielded only a weak *C* effect (7%), and when nested models were compared to the full model, the familial component failed to reach significance. That is, both *A* and *C* could be simultaneously dropped without a significant reduction in model fit, suggesting that

DE is affected by neither genetic effects nor shared factors in the twin/sibling environment. Finally, given that DE is a rare condition in the population, it may be that it takes a very large sample to achieve sufficient power to reliably establish the genetic and environmental effects on DE.

4.5.4 Effects on the continuity of premature ejaculation (Study IV)

The bivariate solution (which was an *AE* model, as no significant *C* effects were detected in the univariate models) revealed a very robust genetic correlation between PE during the first intercourse, and PE at present (r_g = .989), suggesting that more or less exactly the same genes that contribute to PE during the first intercourse are contributing to PE later in life as well. Interestingly, however, very little of the variance between the non-shared environmental components (*E*) of the phenotypes was shared (r_e = .111), suggesting that non-stable or situational effects may be active. It should be noted, that the *E* component is also inclusive of measurement error so that if different sources of measurement error affect the recollection of PE during the first intercourse and the reporting of current PE, the non-shared environmental correlations will be lower. The proportion of the phenotypic correlation between the variables measuring PE during the first intercourse and PE at present that was explained by shared genetic effects was 29.3%. A bivariate model with PE during the first intercourse and DE at present was also investigated, revealing a modest negative association between the two phenotypes; that is, that those who experience PE during the first intercourse are less likely to report DE later in life. 94.8% of the variance in this model was explained by non-shared environmental effects. The correlation between the non-shared environmental components of PE during the first intercourse and DE in the model was negative, and modest (r_e = -.092, [95% confidence interval = -.218 - .014]). Only the *E* component was individually significant, but a significant familial effect was suggested in that the *A* and *C* components could not be dropped simultaneously.

4.6 Ejaculation latency time (Study V and VI)

As ejaculation latency time, or particularly intra-vaginal ejaculation latency time (IELT) has emerged as the predictor of PE around which most of the literature on diagnostics and definition is centered (e.g. McMahon et al., 2008), some results concerning this measure alone is presented below. The term IELT is not used in the present study as the variable measuring latency time was inclusive of anal sex, in order not to exclude homosexual individuals or heterosexuals practicing anal intercourse.

4.6.1 Associations with age and relationship length (Study V and VI)

In both Study V and VI, ejaculation latency time had a very modest, but significant negative correlation with age (r = -.11 and -.12; respectively). In other words, ejaculation latency time seems to decrease slightly with increasing age. In Study VI, an almost identical association with relationship length was detected (r = -.122, p < .001). Together, age and relationship length had an effect size of R^2 = .019, explaining 1.9% of the variance in ejaculation latency time, with both having significant and negative associations when controlling for one another, again meaning that ejaculation latency time is likely to decrease with both increasing age and relationship length; irrespective of the other variable.

4.6.2 Associations with other indicators of ejaculatory function and sexual distress (Study V)

Ejaculation latency time generally displayed very weak to moderate associations with other indicators of PE (see section 3.3.2, or Table 1 of Study V), with significant correlations ranging from r = .16 to r = .42. Interestingly, the strongest correlation was with the variable measuring subjective experience of PE (r = -.42, p < .001), indicating that the likelihood of perceiving oneself as suffering from PE is increasing with decreasing ejaculation latency time. The correlation with number of thrusts was a mere r = .16 (p < .001), indicating that latency time and stimulation are not very strongly related.

4.6.3 Effects of frequency of sexual activities (Study VI)

The results of the analyses investigating effects of the frequency of sexual activities were generally weak (in terms of effects), and somewhat inconclusive. In the correlation analyses, the frequency of all sexual activities (i.e. partnered as well as masturbation) had a significant and positive association with ejaculation latency time, with the exception of vaginal intercourse (an analysis of partial correlations with other sexual activity variables, however, yielded a positive and significant correlation for vaginal sex as well, but not masturbation). In other words, ejaculation latency times seemed to increase with an increasing frequency of all sexual activities bar vaginal sex. In the Complex Samples General Linear Model (CSGLM) regression procedure of SPSS, however, only frequencies of oral and anal sex could significantly predict ejaculation latency time, again with a positive association, so that increasing frequency of sexual activity predicted longer ejaculation latency times. In summary, frequency of oral and anal sex emerged as the only significant predictors of

ejaculation latency time in all analyses, and even for these variables, associations were modest.

The effect of sexual orientation on the frequency of engaging in anal sex was also investigated. Of the not exclusively heterosexual participants, 53.7% reported that they did not engage in anal intercourse. Of the exclusively heterosexual participants, 80.4% reported not participating in anal intercourse. The difference between these groups was significant (t[3076] = 10.875, $p < .001$).

4.6.4 Effects of modes of achieving ejaculation (Study VI)

Results were even more inconclusive for the effects of different modes of ejaculation. Having achieved ejaculation through anal sex was the only predictor of ejaculation latency time to achieve significance in all analyses (correlations, partial correlations and CSGLM regression), again with effects of modest size ($r = .034$, $p < .05$; $r_{partial} = .093$, $p < .001$; $B = 0.194$, $t = 4.350$, $p < .001$). The associations were positive in all analyses, meaning that having achieved ejaculation through anal sex was associated with having generally longer ejaculation latency times.

4.7 Relationship between ejaculatory dysfunction and sexual distress (Study V)

All PE indicator variables had a significant association with experiencing sexual distress, and significant differences between intra-variable levels were detected for several variables. A decomposition of the association of these variables with sexual distress down to the level of individual variable categories can be seen in Table 3 of Study V. The variables "subjective experience of PE", "tried to slow down intercourse", and "worrying about PE" appeared particulary well suited to distinguish different levels of sexual distress, with each variable having significant differences between intra-variable levels. Correlations ranged from $r = .08$ to .37 between the sexual distress scale and the PE indicator variables, and were significant for all variables bar the variable measuring number of penile thrusts. However, only two variables could significantly predict sexual distress when the effects of the other PE indicator variables were controlled for: those measuring "subjective experience of PE", and "worrying about PE". In other words, these two variables had unique variance that contributed to sexual distress that was not shared with any of the other variables. The combined effect size of all PE indicator variables on sexual distress was $R^2 = .165$, indicating that the bulk of the variance in experienced sexual distress is explained by something else than ejaculatory dysfunction.

5 DISCUSSION

5.1 Prevalence of premature and delayed ejaculation (Studies I-III)

Prevalence estimates from the population-based sample of Finnish men in the present study were very much in line with what has previously been published about PE, depending on whether subjective experiences (Montorsi, 2005) or ejaculation latency time (Waldinger, 2005d) was used to distinguish individuals suffering from PE. It should be noted, that ejaculation latency time was self-reported (i.e. not measured with a stopwatch) in the present study, which may cause bias in that particular measure. It is reassuring (in addition to achieving similar results to stop watch studies), however, that there are also indications that stopwatch measured and self reported IELTs are interchangeable, at least for diagnosing PE according to DSM-IV standards (Rosen et al., 2007). In the present group of studies, DE also occurred in numbers comparable to what has been reported elsewhere (e.g. Jannini & Lenzi 2005; Perelman & Rowland, 2006). Results were also similar between the studies, which is partly attributable to overlapping samples between some of the studies (see the Method section for a detailed description of sampling procedures).

5.1.1 Premature ejaculation during the first intercourse (Study I)

Previous studies that have employed IELTs of less than 1 minute to define PE have found prevalence rates of around 1%, or slightly less, in the general population (e.g. Waldinger, Zwinderman, Olivier, & Schweitzer, 2005). Even taking potential recollection bias into account (participants were asked to estimate whether they had ejaculated within one minute at the time of their first sexual intercourse), the number of participants reporting having ejaculated within the minute (29.5%) is quite striking in comparison. As age effects are rather small, and actually indicate that (at least some indicators of) premature ejaculation would become more severe with increasing age, the cause of this is intriguing. It may be the case, that sexually naïve men are more prone to PE because of the expectations and anxieties that accompany the first sexual experiences. It is plausible to assume that age effects on indicators of PE during adulthood and differences in frequency of PE between the first intercourse and later in life are not caused by the same factors. A biological explanation cannot be completely ruled out, however. For example, endocrine causes related to puberty may have an impact on ejaculatory functioning as well (increased levels of testosterone in PE patients have recently been reported by Corona et al., 2008). Anteportal ejaculation occurred with a frequency of 3.7%, which is around three times more often than in PE measured later in life.

5.1.2 Current premature ejaculation (Studies II, III and V)

Less than 2% of the men in the present study reported having an ejaculation latency time of less than a minute, which corresponds quite well with the results of a multinational population study, which reported a prevalence of slightly less than 1% for IELTs < one minute (Waldinger, Quinn et al., 2005). Given that the data in the present study is self-reported, the slight discrepancy may very well be due to response bias in the present sample. On the other hand, a stopwatch in itself may be stressing and add additional pressure to a PE patient participating in a study, and thus result in unusually short IELTs in studies where they are used. Measures of subjective experience are somewhat more difficult to compare, but it is consistent with previous findings that PE prevalence rates increase quite dramatically if a subjective experience and distress is preferred as diagnostic criteria over an IELT of, say, one or two minutes. In Study II, 35.7% reported not having control over their ejaculation in more than half of intercourses, which is quite consistent with figures reported elsewhere (e.g. Montorsi, 2005). Also in Study II, 41.5% felt that they "usually", or "always or nearly always" ejaculated too soon, suggesting that a lot of men are displeased with their ejaculatory performance. Anteportal ejaculation, in general, occurred with a frequency of slightly above 1% (i.e. was reported to occur in more than 50% of intercourses). However, around one in five participants reported to experience anteportal ejaculation at least occasionally which is, given that these studies were conducted on a population-based sample, a quite substantial number.

5.1.3 Current delayed ejaculation (Studies II, III and V)

In the literature, DE is consistently presented as a quite rare condition (Jannini, Simonelli, & Lenzi, 2002; Jannini & Lenzi, 2005; Perelman & Rowland, 2006). In the present study, anejaculation had prevalence rates ranging from 0.2-1.4%, with respondents "usually not ejaculating during intercourse" being somewhat more common, appearing with frequencies within 0.4-2.6%, confirming the relative rarity of DE. DE also had a significant negative association with PE during the first intercourse (r = -.163, p < .001), suggesting that those who suffer, or perceive themselves as suffering, from PE during the first intercourse are less likely to develop DE later in life. Given that PE during the first intercourse was affected by genetic effects, and that no such effects were detected for DE, this implies that environmental factors alone are contributing to the continuity in DE. This is in contradiction to the ejaculation distribution theory (Waldinger & Schweitzer, 2005), which stipulates that ejaculatory function should be viewed as a continuum of latency time, where genetic and neurobiological causal factors are active in the extreme ends of this distribution, causing (lifelong) PE and DE, respectively.

5.2 Effects of age on premature and delayed ejaculation (Studies I-VI)

There has been some confusion regarding the impact of age on ejaculatory dysfunction, however, most empirical studies have found age effects to be rather negligible. It should be noted, though, that PE studies are often conducted either on clinical samples (i.e. PE patients), or quite small samples, and thus small but significant age effects may have gone undetected. In the present group of studies, small but significant positive associations with age were found, but not consistently, thus lending support to the results of Waldinger and his associates, who noted that age has a barely measurable effect on IELT which, if anything, seems to make PE problems slightly worse (Waldinger, Quinn et al., 2005). Still, fairly recently published studies have produced contradicting results and reporting diminishing PE problems with age (e.g. Fasolo et al., 2005; Papaharitou et al., 2006). These contradictions may be another result of different definitional approaches: for example, PE diagnosed according to DSM-IV criteria (i.e. largely subjective reports) may actually be somewhat relieved with age, as the patient comes to terms with and accepts his relatively short IELT, which in itself does not change as he grows older. However, we found no significant moderational effect of age on the association between ejaculation latency time and sexual distress, indicating that the distress related to ejaculation latency time is stable over time. Results for DE were quite similar to those of PE. In Study II, no significant effects of age on DE were detected, but some inconclusive (and weak) indications of a positive association between age and DE were detected in Study IV.

No studies have been conducted on the ejaculatory function of under-18-year-old boys. As most males experience their sexual debut at a younger age than that (e.g. $M = 17.71$, $SD = 2.77$ in the present sample), potentially strong age effects in adolescence may go undetected. Furthermore, bearing in mind the enormous discrepancy in prevalence rates of ejaculating within one minute between the first sexual intercourse and later in life (29.5% vs. <2%), there may also be profound effects of sexual naïvete (rather than age itself) on PE, which should indeed be investigated further. For example, it may be that substantially elevated levels of anxiety and sexual excitation are causing PE in the sexually naïve.

5.3 Effects of sexual orientation on premature and delayed ejaculation

Sexual orientation as a factor that could potentially affect ejaculatory function has been rather overlooked in the literature. This is surprising, especially in the context of the vigorous attempts to formulate universally suitable definitions for PE (and DE)

that have taken place recently. For example, the definition of lifelong PE as proposed by the ISSM (McMahon et al., 2008) does specifically stipulate a diagnostic criterion of *vaginal* penetration of less than one minute, which effectively excludes homosexual sexual interactions.

In the present study, sexual orientation was found to be associated with higher levels of DE whereas it had no association with PE. However, the effect on DE disappeared when the analysis was recomputed while controlling for the frequency and type of sexual activity which in their turn varied with sexual orientation. Since different sexual activities (and the frequency with which these activities occur) can affect ejaculatory function, the effects of sexual orientation on ejaculatory function seem to be mediated by differences in these actitivities.

5.4 Associations between premature ejaculation at the first sexual intercourse and current premature and delayed ejaculation (Study IV)

No proper longitudinal study of ejaculatory function has been conducted. At best, clinical trial studies have followed a sample over a few weeks (e.g. Pryor et al., 2006). The rest of the evidence for continuity of PE stems from self-reports of patients and indirect sources (e.g. a study pointing out that behavioral therapy to treat PE has little effect in the long term). In the present study, the continuity and stability of PE was investigated by comparing self-reports of PE at the first sexual intercourse with self-reports of current ejaculatory function. This, then, may be vulnerable to response bias: a participant currently suffering from PE may be more inclined to believe that he has "always" suffered from PE, even if this has not necessarily been the case. Furthermore, participants' recollections may not be accurate if several years (or even decades) have passed since the first sexual intercourse. In other words, results achieved under circumstances like these should be treated with necessary caution and common sense; however, some interesting findings may be gained from results such as these as well. The rather overwhelming superiority with which an ejaculation latency time of less than 1 minute was reported during the first intercourse (Study I) than later in life (e.g. Studies II and III) – 29.5% vs. less than 2% for any numbers not derived from data on the first intercourse – surely has some implications that need to be seriously considered. It is intriguing to speculate what is causal of such a vast difference between the first intercourse and later intercourse events. It could be, that different levels of sexual excitation, or anxiety, are (at least partly) causal. Given that most people are adolescents at the time of their first intercourse, differences in hormonal levels as a result of puberty may also be involved. Nevertheless, it appears that suffering from PE-related problems during the first intercourse does not predict PE later in life very accurately, at least when diagnosed by 1-minute IELTs. As little

is known about sexual dysfunctions in men during only the first intercourses, it may be that "dysfunctions" such as PE are far more common in sexually naïve men, and that this "dysfunction" can be considered a normal phase in a man's sexual development, even though his "symptoms", in principle, fulfill the criteria for any proposed diagnosis of PE. However, it should be borne in mind that PE during the first intercourse and current PE had a moderate and highly significant positive correlation between them ($r = .340$, $p < .001$), indicating stability over time for this variable as well. Individuals with a genetic vulnerability for PE symptoms are vulnerable also at the first intercourse. Most of the variance in PE is, nonetheless, explained by individually unique environmental factors, thus calling the validity of predicting PE later in life based on the occurrence of PE during the first intercourse into question.

5.5 Genetic and environmental influences on premature and delayed ejaculation (Studies I-IV)

Although genetic effects on ejaculatory function have been suggested, and certainly not unfoundedly, in the literature (e.g. Schapiro, 1943; Waldinger, Rietschel et al., 1998), investigating (particularly the amplitude of) genetic influence on PE and DE was rather uncharted territory prior to the commencement of this study. Nevertheless, there was reason to be optimistic in the pursuit of evidence for a hereditary etiology to PE and DE. Preliminary analyses (phenotypic correlations) suggested a partial genetic etiology to PE, but not DE.

5.5.1 Premature ejaculation during the first intercourse (Study I)

Genetic model fitting analyses revealed a significant genetic effect on PE during the first intercourse accounting for around 22% of the total phenotypic variance, with the rest of the variance accounted for by non-shared environmental effects. Of the potential non-shared environmental effects that contributed to variance in PE, alcohol use and having sex with an unknown partner both decreased the occurrence of PE. Alcohol, thus, seems to have an inhibitory action on ejaculation, confirming previous research (Malatesta et al., 1979). Affect, both positive and negative, were on the other hand found to increase the occurrence of PE, implying a mediational role for affect in how contextual factors affect sexual dysfunction during first intercourse. This may be related to levels of sexual excitement, which could be significantly higher for the novice compared to general levels of sexual excitement during sexual activities in more experienced men.

5.5.2 Current premature ejaculation (Studies II-IV)

Inconclusive evidence for a (partial) genetic etiology to PE could not be generated from the data available for Study II, although it did provide strong implications for a significant additive genetic effect. In the subsequent Study III, with improved statistical power, a highly significant genetic effect was found, providing the first reliable inconclusive evidence of a genetic etiology to PE. At first glance, it may seem odd from the evolutionary perspective that a sexually (and thus reproductionally) related trait that is generally perceived as a dysfunction and leads to having fewer partners and less frequent sexual intercourse would have a (partially) genetic etiology. That is, if some genes would have harmful effects on reproductive fitness, those genes should be eliminated from the gene pool because of natural selection. However, as Hong (1984) pointed out, ejaculatory quickness may have been an advantageous trait, reducing the likelihood to be repelled by females or attacked by other males in the development of humans, and also allowing less dominant males to reproduce. This may still be observed in primates. If so, it is questionable whether any ejaculation latency time (except perhaps one so short it would always cause ejaculation *ante portas*) can ultimately be classified as dysfunctional. In other words, if there are no direct advantages to longer copulation, a long ejaculation latency time can actually be perceived as a risk factor in itself. There are some indications that successful conception is more likely if the female achieves orgasm (Baker & Bellis, 1993), however, such indications have also been disputed (e.g. Lloyd, 2005). One potential evolutionary advantage of longer copulation could thus be that it allows more time for the female partner to achieve orgasm. Given that less than one per cent of the participants in the present study reported that they suffered from anteportal ejaculation, the frequency of PE that could be considered a disturbance in an ultimate sense seems to be very low. This is to be expected as there would be strong selective pressure against alleles that contribute to anteportal ejaculation. An interesting question is whether the etiology of anteportal ejaculation differs from that of short ejaculation latency time.

The establishment of a (partial) genetic etiology for PE is an important finding, but it does not in itself reveal much about the actual biological mechanisms causal of PE. Presently available data do suggest that PE is caused by centrally (i.e. brain level) active mechanisms, which is implied in that neurotransmitters such as serotonin and dopamine seem to be involved in ejaculatory functioning. The only genetic polymorphism study published to date (Janssen et al., 2009) did report significant allele effects of the *5-HTTLPR* polymorphism on IELT in a group of PE patients, however, no differences in allele frequencies between PE patients and controls were found. In other words, one cannot confirm that any allele of the *5-HTTLPR*

polymorphism would be directly causal of a shorter ejaculation latency time. Furthermore, SSRIs do have a proven ejaculation-delaying effect, which lends some support to the involvement of serotonin in the ejaculatory response. However, SSRIs have also been found to significantly reduce libido and sexual pleasure (e.g. Corona et al., 2009), which may instead be the causal factors of increased IELTs, rather than the increased levels of metabolic serotonin itself. Furthermore, an association between a central mechanism (e.g. serotonin regulation) and an observable trait (e.g. PE) does not exclude environmental causality: for example, a hormonal effect *in utero* or some other environmental factor early in the development may (at least theoretically) cause variations in serotonin regulation and receptor activity. Indeed, this mechanism has been shown for some aspects of aggressive behavior in rats (van Riel, van Gemert, Meijer, & Joëls, 2004). In turn, such a mechanism could also contribute to variations in the ejaculatory reflex.

The endophenotype behind PE may also be a more peripheral mechanism. There is no clear-cut evidence of any substantial variations in ejaculatory functioning due to differences in glans penis sensitivity, or that circumcision status would have any considerable impact on ejaculatory functioning. However, topical treatments – while certainly having some disadvantages of their own – have been demonstrated to successfully delay ejaculation (Morales, Barada, & Wyllie, 2007), suggesting that variations in peripheral sensory input cause variations in ejaculation latency times. A group of cells in the lumbosacral spinal cord hypothesized to relay ejaculation-triggering peripheral signals to the central nervous system have been described by Truitt and Coolen (2002), also indicating that peripheral mechanisms are of importance to the ejaculatory reflex.

Most of the variance in PE is, however, caused by non-shared environmental effects, most of which are still unclear. It should be noted, however, that the non-shared environmental component *E* also contains measurement error. Thus, any flaws in the measurement of PE could lead to underestimation of additive genetic effects. In other words, the genetic effect on PE could be substantially higher than has been measured in the present group of studies.

5.5.3 Current delayed ejaculation (Studies II-IV)

The results of model fitting analyses on DE were somewhat inconclusive, but most indicators point to DE having an etiology unaffected by genes. The analysis conducted on the largest sample indicated that neither familial components (*A* or *C*) had any significant influence over DE. From the evolutionary point of view, this is sensible: it is hard to think of any reason why a gene causing anejaculation or

delayed ejaculation would survive natural selection. This is also largely in line with what has previously been published regarding the etiology of DE, namely that it in most cases is a side-effect of drugs, physical trauma, or a complication of surgery or various medical conditions (Segraves, 1989; Rosen, 2000). While it is established that ejaculation is a reflex dependent on neuronal functioning (Truitt & Coolen, 2002), a genetic mutation disruptive of this reflex would surely have slim chances of survival. This has some implications for the ejaculation distribution theory (Waldinger & Schweitzer, 2005). While it is tempting to view PE and DE as extremes on opposite sides of an ejaculation latency time distribution, this view may not necessarily contribute much to the understanding of the etiology of DE. In other words, it does not seem that the etiology of DE is simply the inverse of the etiology of PE. However, current DE had a significant negative association with experiencing PE during the first intercourse. Being intoxicated and having sex with an unknown partner were both negatively associated with suffering from PE during the first intercourse, suggesting that these two could be environmental factors that contribute to delayed ejaculation. In addition, because DE occurs with a very low frequency in the population, random effects may show in the model fitting analyses as any particular concordant or discordant sibling pair will have a proportionally large effect on the estimation of genetic effects if the few participants reporting DE happen to be discrepant with regards to some other variable by chance.

5.5.4 Effects on the continuity of premature ejaculation (Study IV)

In the present study, a genetic correlation of (r_g = .989) was found between PE during the first intercourse and current PE. This indicates, quite clearly, that the genes that cause vulnerability to PE during the first intercourse are the same that contribute to PE later in life. However, the correlation between the non-shared environmental components of PE during the first intercourse and current PE was a mere r_e = .111, suggesting that very different environmental causal factors are behind PE later in life. However, given that the all measurement error is modeled in the *E* component, it may be that this correlation is underestimated. Given that the majority of the variation in PE both during the first intercourse and later in life is caused by non-shared environmental effects, it is intriguing and interesting that the correlation between both *E* components is so dramatically low. Certain contextual factors (such as performance anxiety, peer pressure or perhaps intoxication) may have a greater impact on the first intercourse than they would later in life, supporting the notion that while PE may not necessarily be affected by age, sexual naïvete may instead have a profound effect on ejaculatory functioning. Also, a prolonged spell of sexual failure may become a vicious circle; in other words, become causal of dysfunction in itself. This argument is also plausible in the case of DE. If true, this would not have

an impact on the first sexual intercourse. The participants were asked to evaluate their ejaculation latencies at the first intercourse retrospectively, and potential response bias could perhaps be expected especially from those who currently (feel that they) suffer from PE. However, if true, this should cause an increase in the non-shared environmental correlation r_e, which at .111 is considerably low.

5.6 Ejaculation latency time (Study V and VI)

As IELT has emerged as the indicator of PE around which new definitions are to be centered (McMahon et al., 2008), it may be worthwhile to consider ejaculation latency time separately in some contexts. It should be noted that the measure of ejaculation latency time in the present group of studies did not differentiate further between ejaculation latencies beyond "more than 10 minutes" ("I do not ejaculate during intercourse" is, however, included as a category). In other words, it is designed and more suitable for the shorter ejaculation latency times (that is, PE) while it cannot separate those who have "normal" ejaculation times from those who have abnormally long, but still do ejaculate. Furthermore, latency time in itself is not a direct measure of stimulation, which may be perceived as another weakness of ejaculation latency time as a measure of PE, which was also evident by its low correlation with the number of penile thrusts ($r = .16$, $p < .001$).

5.6.1 Associations with age and relationship length (Study V and VI)

Confirming the results of some previous studies, ejaculation latency time was found to have slight negative association with both age and relationship length (Waldinger, Hengeveld et al., 1998b). Effects were generally very small, and it may very well be that age and relationship length are unlikely to be relevant in the clinical setting. However, it is intriguing to speculate on why relationship length seems to decrease ejaculation latency times in men. In women, it has been shown that sexual distress increases with growing relationship length (Witting et al., 2008). Should the same pattern hold true for men as well, it may be that men consciously attempt shorter intercourses in order to avoid an unfulfilling sexual relationship. It may also be, that sex can become more perfunctory over time in a relationship, and thus less effort is put into the maintenance of a well-functioning sexual relation.

5.6.2 Effects of frequency of sexual activities (Study VI)

Almost nothing is known about how frequency of sexual activities (other than vaginal intercourse), or indeed how other sexual activities *per se* affect ejaculatory functioning. As human sexual behavior is varied and not limited to (heterosexual)

vaginal sex, there is good reason to look into potential effects of different sexual activities, and whether the frequency of these activities have an impact on ejaculation latency time.

More frequent involvement in sexual interaction was indicative of longer ejaculation latency times for all sexual activities, particularly oral and anal sex. However, no conclusions with regards to causality can be drawn based on these results – it may be the case that dysfunctional men become avoidant of sex, and thus less frequently engage in intercourse.

5.6.3 Effects of modes of achieving ejaculation (Study VI)

Other sexual activities, particularly anal sex, were associated with longer ejaculation latency times in the present study. Again, caution is advised in the interpretation of these results, as it may be that men with longer ejaculation latency times are more sexually adventurous than their counterparts. While effects were generally quite modest, these findings do imply that there may be some benefits to practice and variation. But if a more varied and frequent involvement in sexual interaction is indeed causal of a longer ejaculation latency time, this finding may have some therapeutic implications: possibly, (in the less severe cases of PE), a varied foreplay (e.g. oral sex or manual stimulation; as anal sex would probably not be regarded as foreplay by most couples) could potentially reduce PE problems during penetrative sex. Furthermore, involvement in certain sexual activities may be due to variation in sexual orientation. In the present study, participants who were not exclusively heterosexual were engaging in anal sex significantly more frequently than their exclusively heterosexual counterparts, however, there was no information available whether the non-heterosexual participants were the ones penetrating or being penetrated, or both.

It is also conceivable that vaginal sex is causal of shorter ejaculation latency times compared to other modes of ejaculation, for several reasons. Firstly, the vagina has a lot of muscles (compared to the anal or oral cavities) within it, and may as such offer more physical stimulation than the other orifices. Secondly, from the evolutionary perspective, it may generally be perceived as more arousing to penetrate the vagina than any other orifice, as the vagina makes conception possible. Furthermore, it may be that vaginal sex is more related to performance anxiety for the same reason.

5.7 Relationship of ejaculatory dysfunction and sexual distress (Study V)

Variables indicating ejaculatory dysfunction had, on the whole, surprisingly weak associations with sexual distress, especially so when considering that quite strong associations between PE and distress have been reported previously. For example, Patrick et al. (2005) found in a convenience sample of 1,587 individuals (of which 207 were diagnosed with PE by DSM-IV criteria) that 64% of PE patients reported ratings of "extremely" or "quite a bit" for personal distress compared to 4% of non-PE men. Only two variables, both of which were indicative of subjective experience of PE, had unique effects that could significantly predict sexual distress (that is, when the other variables were simultaneously controlled for). This association could be indicative of general distress (e.g. persons going through stressful life events may also perceive their sexual lives as distressing). With a combined effect size of 16.5% between all the variables, more than four fifths of the variance in experienced sexual distress seems to stem from other sources than PE and DE. It is rather intriguing that PE does not seem to have any particularly strong relationship with sexual distress, and also somewhat contradictory to reports that PE has a profound negative effect on a man's (sexual) life (e.g. Hartmann, Schedlowski, & Krüger, 2005), at least if defined by objective measures such as ejaculation latency time. On the other hand, a man may be distressed and unhappy with his ejaculatory latency time in general, while still having fully normal or even very long ejaculation latency times (Waldinger & Schweitzer, 2008b). In other words, a man may be distressed without dysfunction, or dysfunctional without distress, or indeed any combination of the two. As most of the variation in sexual distress is coming from somewhere else than ejaculatory dysfunction, it may be that sexual distress is foremostly related to the partner relation, and general psychopathology. It is also questionable whose distress is measured when it is in relation to a short ejaculation latency time – the distress experienced by the quickly ejaculating man himself does probably not reflect a reduction in sexual pleasure *per se*, but sexual distress in his partner (partners of men diagnosed with PE report significantly more personal distress than partners of non-PE men; Patrick et al., 2005), and maybe their relationship as a consequence of that. If, for example, a quickly ejaculating man had a partner who continuously expressed joy for his ejaculatory swiftness, he would not necessarily perceive his short ejaculation latency time as distressing. Finally, other sexual dysfunctions (that is, other than PE or DE) could contribute to the variance in sexual distress. It may be, for example, that erectile dysfunction has a comparatively larger impact on sexual distress. Interestingly, erectile dysfunction and PE appear to be correlated (e.g. Jannini, Lombardo, & Lenzi, 2005).

Significant intra-variable level differences were also detected for several variables in association to sexual distress, indicating that ejaculatory problems may become considerably distressful only if a certain threshold is reached. For example, it may be that experiencing PE "often" is not particularly distressing, whereas "always" is. While it was generally variables measuring subjective experience of PE that had clear-cut intra-variable level differences in terms of sexual distress, significant differences were also found between the levels of more "technical" variables such as ejaculation latency time. Bearing the diagnostic criteria of PE in mind, it may be that subjective criteria are better able to capture and distinguish dysfunction if the levels of subjective measures are considered.

The variables indicating ejaculatory function were also reasonably poorly intercorrelated, indicating that several different aspects of ejaculatory functioning were captured and measuring of single aspects, such as, ejaculation latency time, is insufficient for the understanding and diagnosis of PE.

5.8 Implications for diagnostics and treatment

Temporal stability of PE is assumed in the new definition and diagnostic criteria for life-long PE proposed by the International Society of Sexual Medicine (McMahon et al., 2008), but no properly conducted longitudinal study has actually investigated how ejaculation latency time behaves over time, and many potential variables that could affect ejaculatory performance (such as the role of foreplay, or having different partners) have also eluded scientific scrutiny. If there are indeed profound effects of sexual inexperience on ejaculation latency time (be reminded, that almost 30% of the men in the present study reported ejaculating within one minute during the first intercourse), it can be that this effect is non-permanent but very much present at the first handful of sexual encounters, or with different partners. This could, for example, see a quite normally functioning teenager fulfill all diagnostic criteria for lifelong PE.

In the present study, it appears that there is a negligible association between measures of more objective nature (such as ejaculation latency time and number of thrusts). While it appears that the two are unrelated, there are disadvantages to preferring the one over the other. If diagnosis in based solely on objective measures, such as IELT, men who are perfectly happy with their condition will be defined as dysfunctional. On the other hand, if diagnosis is based on subjective measures, "normally" functioning men who complain about PE may receive unnecessary treatment. An overview of the pros and cons of subjective and objective measures can be seen in Figure 2.

Objective measures	*Subjective measures*	
	Yes	**No**
Yes	+ both distress and a quantifiable, objective measure are captured - subjective and objective measures are not strongly associated, leading to difficulties e.g. when only either measure is indicative of dysfunction	+ is quantifiable and advantageous in the research setting - does not define dysfunction on an ultimate level, still requires on an subjectively chosen threshold, which does not capture distress very well
No	+ captures sexual distress and thereby measures well-being in the individual - fails to separate complaints of individuals with ”normal” function by objective measures from those with dysfunction	

Figure 2. Cross tabulation describing advantages and disadvantages of subjective and objective measures of ejaculatory function for the diagnosis of ejaculatory dysfunction.

Inadequate diagnostic criteria have other implications as well. Erectile dysfunction medication has, for instance, become hugely popular, and reports have shown that the majority of the erectile dysfunction medication is consumed for recreational, rather than medicinal, purposes (Santtila et al., 2007). Furthermore, in a study of college students, it has been shown that most erectile dysfunction medication users have not obtained their pills from a physician (Mussachio, Hatrich, & Garofalo, 2006). As many men perceive themselves as having ejaculatory dysfunction, or are disappointed in their ejaculatory performance, it is rather safe to assume that there will be a strong demand for PE drugs, especially among the young. Given the potentially harmful side effects of SSRIs, which are commonly used in PE treatment (e.g. Corona et al., 2009), unnecessary drug prescriptions due to ill defined definitions can be more harmful than beneficial. However, it must be maintained, that the (effective) drugs becoming available is a positive thing for many men suffering from PE – but it does not mean that the issues regarding definition, etiology and diagnostic criteria have been resolved.

The effectivity and suitability of SSRI medication in the treatment of PE has also been questioned in the literature. For example, the only label drug available so far for on-label PE treatment, the on-demand SSRI dapoxetine, has been criticized for being comparatively uneffective (Waldinger & Schweitzer, 2008a). Dapoxetine, at best, has a 4.43-fold increase in IELT (for all patients, the IELT increase with the highest trial dose was 3.32-fold at the end of the study), which would increase an IELT of 30 seconds to just above two minutes (Pryor et al., 2006). Longer IELTs have been

achieved in trials with other SSRIs, particularly paroxetine with an almost 15-fold mean IELT increase (Waldinger et al., 2004). However, SSRIs in general have been found to significantly decrease libido as well as pleasure related to both masturbation and partnered sexual activities (Corona et al., 2009; Balon, 2006), in addition to many other negative side effects of SSRI medication that have been widely reported, such as lethargy, fatigue and sleep disturbances (e.g. Sherman, 1998). Thus, the reduction of libido and perceived pleasure may be the principal ejaculation-delaying factor. While it is conceivable that a man who has suffered from severe PE all his life may be welcoming any delay in his ejaculation, it is debatable whether SSRI medication is a good option for most patients in the long run. Furthermore, there are some indications that most clinical trials with SSRIs for PE treatment are flawed. For example, out of 79 studies included in a meta-analysis published in 2004, only three had a three-digit sample size (Waldinger et al., 2004). Furthermore, recent studies with large samples have been criticized for being influenced by interests of research-funding pharmaceutical companies (Waldinger & Schweitzer, 2008a).

It has also been proposed in the literature, that PE only has a "biological" or "genetic" etiology if it is "lifelong", with "acquired" PE (which is developed later in life) being more attributable to "psychological or relationship problems" (as well as secondary to other conditions; McMahon et al., 2008, p. 1590) among other causal factors. However, "psychological problems" such as anxiety and mood disorders have a substantial genetic etiology, and this has been known, or at least suspected, for decades (Plomin et al., 2001). Furthermore, there is substantial evidence for the involvement of the short allele of the serotonin transporter gene *5-HTTLPR* in developing depression as a consequence of distressing life events (e.g. Caspi et al., 2003; Kendler, Kuhn, Vittum, Prescott, & Riley, 2005), and also some evidence for its involvement in the development of anxiety spectrum disorders (e.g. Bengel et al., 1999) - the very same allele has recently been shown to have some association with lifelong PE (Janssen et al., 2009). Additionally, the term "lifelong" (McMahon et al., 2008) is somewhat misleading, in that men are not sexually active, and certainly not eligible for study participation, all their lives. It may, thus, be plausible to assume a biological component to have an impact on ejaculatory function in general, and not just for a subtype with assumed very early onset.

It is also somewhat surprising that no PE or DE studies have focused on the whole picture of (partnered) sexual interplay when investigating ejaculatory function. For example, recent research and definitions have focused on Intra-vaginal Ejaculation Latency Time – but no IELT study has ever taken into account how foreplay, which can surely be assumed to be fairly common, might affect IELT. With the employment

of IELT only comes the assumption that latency time-affecting sexual interplay starts at penetration, and ends at ejaculation.

Finally, it may be worthwhile to consider why remarkably less effort is put into investigating the etiology and potential treatment of DE. One reason is surely the low frequency with which it occurs in the population. However, it may also be that DE, because it may be less distressing for the partner, does not raise similar concerns. For example, if there is an ideal among men (and women) that men should be sexually endurant, a man suffering from DE may not seek help even though the condition is harmful. Furthermore, DE is certainly easier to conceal than PE, and thus given the tendency among men to be embarrassed to seek help for sexual dysfunctions, DE may actually be more prevalent than studies have shown so far.

5.9 Suggestions for future research

The immediate goal for research on the genetics of PE is to look for functional polymorphisms related to ejaculatory function. There is some evidence for the involvement of the *5-HTTLPR* serotonin transporter promoter region polymorphism, and an effort to replicate the findings of Janssen et al. (2009), and perhaps establish the role of this gene's polymorphisms would be highly important. Still, in relation to the genetics of PE, gene-environment interactions and –correlations should be given some consideration. For example, there is some (albeit inconclusive) evidence for the role of the *5-HTTLPR* gene being related to neuropsychiatric disorders; especially anxiety-related traits (Schinka, Busch, & Robichaux-Keene, 2004). Thus, trauma (such as sexual failure) could contribute more to the development of PE in individuals with certain genotypes. If successful, these studies could be a first step on the way to create genetically tailored drugs to treat PE (i.e. drugs that are more effective if they match a certain genotype; Shin, Kayser, & Langaee, 2009).

The effects of contextual factors, such as variation in ejaculatory function between partners would certainly be received with great interest. Furthermore, it would be important to investigate how variables related to the partner (e.g. perceived attractiveness, or intimidation) affects ejaculatory functioning. Likewise, a properly conducted longitudinal study would also generate highly important findings. Here, the so-called "dynamic P-technique" (in which data is collected from one or a few persons, over multiple time points) could be used in addition to the standard longitudinal procedure. As the results of the present study indicates a very high prevalence of PE during the first intercourse, it would be interesting to study if and how men perceive that their ejaculatory function has changed from their sexual début. Finally, very little is still known about the (non-traumatic or -medical)

etiology of DE. While it is possible that a substantially larger sample than what has been available for the present group of studies is required to get an adequate picture of the genetic and environmental effects on DE, it appears that familial effects have a rather negligible impact on the etiology of DE. On the ultimate level, it makes perfect evolutionary sense that there appears to be no genes causal of (severe) DE, as genes that cause substantial impairment to a man's ability to pass on his genes would quickly be eliminated from the gene pool.

As ejaculation latency time in general, and the variable measuring ejaculation latency time used in the present group of studies in particular, does not provide an empirically reasonable measure of DE, one cannot suggest that a contextual factor negatively associated with latency time is indicative of DE. Likewise, a negative association of any variable with PE does not necessarily indicate DE. However, it is interesting that being intoxicated or having sex with an unknown partner was counterindicative of PE during the first intercourse (at which the frequency of occurrence of PE was very high). It can thus be speculated, that substance abuse and factors in the partner relation could be involved in the etiology of DE.

5.10 Limitations

A few potential limitations of this group of studies should be considered. First, the response rate, which at slightly less than 30% may seem rather low. However, when the extensiveness of the questionnaire (which covered a vast number of instruments on sensitive topics), it must still be considered decent. Furthermore, the numbers are comparable with previously conducted sexuality related mail surveys both nationally (Haavio-Mannila & Kontula, 2003) and internationally (Bailey, Dunne, & Martin, 2000; Långström & Zucker, 2005). Additionally, the present sample is comparable with other representative Finnish population samples on several sexuality related characteristics, such as mean age of first intercourse (Mustanski, Viken, Kaprio, Winter, & Rose, 2007) and rates of sexual abuse (Sariola & Uutela, 1994).

Although the present study was conducted on a twin sample, results are not limited to be valid for twins only. It is well established that twins do not differ significantly from singletons on a number of variables, among those socio-demographic and behavioral characteristics such as depression, somatization and insomnia (Andrew et al., 2001; Johnson, Krueger, Bouchard, & McGue, 2002; Kendler, Martin, Heath, & Eaves, 1995; Pulkkinen, Vaalamo, Hietala, Kaprio, & Rose, 2003). The present group of studies was not exclusively conducted on twins, either (siblings were also

included). Furthermore, most of the results in the present study correspond very well to the results of previously published studies.

In the present group of studies, homo- and bisexual individuals have been included in the analyses, and sexual orientation has not been controlled for (except where mentioned). This may be a distorting factor, but there are also advantages in including any participant regardless of sexual orientation, in that it improves generalizability of the results. Results of additional analyses (i.e. analyses not appearing in any of the six published papers) also indicated that no significant direct effects of sexual orientation on ejaculatory function were present when frequency and type of sexual activity was controlled for.

One of the measures, the Sexual Distress Scale, is developed from a questionnaire intended for (and thus only validated in) samples of women, in which it has been found to have good psychometric properties (Female Sexual Distress Scale; Derogatis et al., 2002). However, as can be seen in Study V, all of the seven questions were gender neutral, and a number of measures were taken to establish concurrent validity in the sample of men.

The intercorrelations between the items measuring different aspects of ejaculatory function were generally low. This is particularly problematic for the formulation of a definition of the problem (i.e. PE, or DE). However, it is also difficult to choose any particular indicator over the other indicators as the individual indicators are associated with different advantages and disadvantages. In fact, most scholars advocate a multi-aspect approach to the definition of PE (e.g. the definition of McMahon et al., 2008).

The association between self-report of current ejaculatory latency and remembered ejaculatory latency at the first intercourse attempt is subject to potential bias, since a man who currently suffers from PE may have a distorted memory of his first intercourse attempt as a result of negative self-perception due to his current condition. Or reversely, a man who currently perceives himself as well-functioning and controlled may exaggerate the ejaculatory latency of his first intercourse as a result of having had complete control of his ejaculation for a long time.

Lastly, gene-environment interactions or –correlations were not tested for. It is possible that, for example, personal trauma or other events may have different effects on different individuals depending on their genotype. In other words, carriers of certain genes and alleles may be more vulnerable to causal agents of ejaculatory dysfunction in the environment.

6 SUMMARY AND CONCLUSIONS

In the present study, ejaculatory dysfunction, and some of its etiology and correlates were studied in a relatively large population-based sample of Finnish male twins and their siblings. It is the first study to empirically explore the genetic etiology of premature and delayed ejaculation. Effects of age, relationship length, different sexual activities and modes of achieving ejaculation were assessed, and currently used diagnostic criteria were considered and evaluated. Its key findings are briefly outlined below according to the aims stipulated in section 2:

1. What is the prevalence rate of PE and DE in a Finnish sample? (Studies I-III)

Premature ejaculation is about as prevalent in Finland as it has been shown to be elsewhere. Prevalence estimates are largely dependent on choice of definitional criteria. Around one in three men report subjective experience of PE, and slightly less than 2% report ejaculation latency times of less than one minute. Delayed ejaculation is significantly less prevalent, with around 2% reporting usually not ejaculating, and an additional two reporting trying to speed up intercourse sometimes. Premature ejaculation is reported substantially more often in the context of the first sexual intercourse, with almost 30% reporting having ejaculated within a minute of intercourse.

2. How are age and relationship length associated with PE and DE? (Studies I-VI)

Age and relationship length generally had weak, but significant positive associations with premature ejaculation. In other words, PE problems seemed to increase with age and length of the relationship. However, large discrepancies between reported very short ejaculation latency times (<1 minute) at the first intercourse and later in life suggest that ejaculatory function is affected by sexual experience, or age effects that may have gone undetected because the ejaculatory function of young adolescents has never been studies. The relationship of delayed ejaculation and age remains inconclusive, however, some analyses indicated a weak, positive association in this case also.

3. How is sexual orientation associated with PE and DE?

In the present study, sexual orientation did not appear to have any direct effects on ejaculatory function. However, frequency and type of sexual activity did vary with sexual orientation, and since the latter can affect ejaculatory functioning, sexual orientation may have an indirect effect on ejaculatory function through mediation of frequency and type of sexual activity. With age as the sole covariate, sexual orientation had a significant effect on DE, so that individuals with homosexual experience had elevated levels of DE-related problems compared to exclusively heterosexual individuals, but this effect failed to reach significance when frequency and type of sexual activity were controlled for.

4. Is there an association between experiencing PE during the first intercourse and suffering from PE later in life? (Study IV)

The present study provided some evidence for continuity over time of premature ejaculation. There were also indirect indications for stability over time for delayed ejaculation. Nonetheless, a well-designed, extensive longitudinal study that takes contextual factors into account is needed to fully understand how PE behaves over time.

5. Are there genetic effects on PE and DE, and if so, how large a proportion of the total variance in PE or DE is under genetic influence? (Studies I-IV)

Premature ejaculation seems to be under moderate genetic influence, with around 30% (or slightly less) of the total phenotypic variance accounted for by genetic effects. The rest of the variance was accounted for by environmental influences unique to the individual. This was true also for premature ejaculation during the first intercourse. No significant genetic or shared environmental effects could be established for delayed ejaculation, although there were some implications for a small familial effect also in DE.

6. Is there anything to suggest that PE is a stable condition over time, and if so, is such stability caused by genetic and environmental influences? (Study IV)

Premature ejaculation during the first intercourse had a moderate and highly significant association with reporting PE later in life. The genetic correlation between premature ejaculation during the first intercourse and later in life was very high,

indicating that the very same genes that contribute to premature ejaculation at the sexual debut are at work later in life as well. On the other hand, very little of the unique environmental factors that contribute to the variance in premature ejaculation were common between the first sexual intercourse and later in life.

7. Are contextual factors affecting PE during the first intercourse? (Study VI)

Intoxication and having sex with an unknown partner were counterindicative of premature ejaculation during the first intercourse. Positive and negative affect, on the other hand, were indicative of PE.

8. Is PE, or any specific indicator of PE, associated with sexual distress, and if so, are there measurable thresholds related to ejaculatory functioning where sexual distress becomes more prominent? (Study V)

Generally, indicators of premature ejaculation had very weak associations with sexual distress, but all bar one indicator had significant associations with sexual distress. When controlling for effects of all variables simultaneously, only variables measuring subjective experience of premature ejaculation could significantly predict sexual distress. In total, premature ejaculation was estimated to account for 16.5% of the variance in sexual distress, meaning that the vast majority of the factors contributing to sexual distress are something else that premature ejaculation. These may be related to the partner relation, or general psychopathology.

9. What are the unique associations of age and relationship length (i.e. of age when relationship length is controlled for, and vice versa) with ejaculation latency time? (Study VI)

Ejaculation latency time had weak, but significant, associations with both age and relationship length, so that ejaculation latency time appeared to become shorter with increasing age and relationship length.

10. Is there an association between ejaculation latency time and frequency of engaging in different sexual activities (e.g. vaginal, anal or oral sex)? (Study VI)

Ejaculation latency time is somewhat affected by frequency of sexual behaviors, and by what means ejaculation has been achieved. Frequent sexual behavior was associated with longer ejaculation latency times, and having oral and anal sex was

also indicative of longer latency. However, no direction of causality is established for these correlates in the present study.

11. Is there an association between ejaculation latency time and achieving ejaculation through different modes (e.g. through vaginal, anal or oral sex)? (Study VI)

Generally, ejaculation latency time had weak associations with different modes of achieving ejaculation. However, while significant associations between ejaculation latency time and several modes, anal sex appeared to have the most robust effect, being associated with significantly longer ejaculation latency times. It was hypothesized, that vaginal sex may be associated with shorter ejaculation latency times partly for physiological reasons: with the vagina being able to contract over a larger area than any other orifice, it may be that the physical stimulation is more effective during vaginal sex. Secondly, an evolutionary explanation could be that men generally perceive vaginal penetration as more arousing because it may lead to conception (and thus, offspring).

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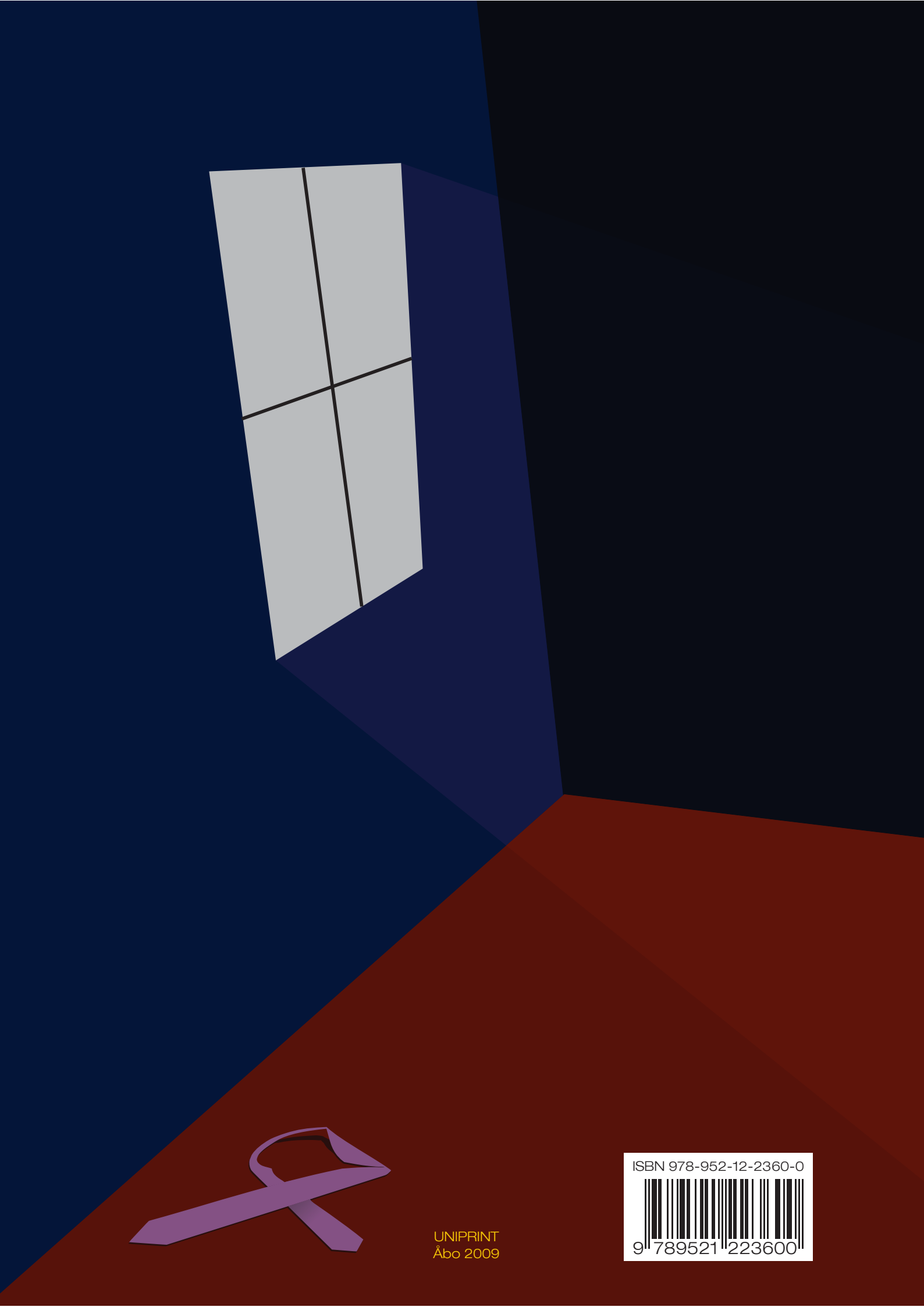

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